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Non-motor Functions Of The Cerebellum

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NON-MOTOR FUNCTIONS OF THE CEREBELLUM

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ABSTRACT

Monkeys, cats, and rats were used to study non-motor behavioral changes after cerebellar manipulation. Monkeys and cats showed changes towards greater "friendliness" and tractability after lesions of the posterior cerebellar vermis. Similar observations were made in kittens which had been subjected to cerebellectomies at an early age. Rats with lesions in the posterior cerebellar vermis differed in their reaction to food, electrical shock, and intracranial self-stimulation (ICSS) from control animals. In addition, stimulation of the anterior cerebellar vermis appeared to facilitate ICSS in rats while stimulation of the posterior vermis appeared to be without effect on ICSS.

The non-motor behavioral changes in monkeys, cats, and rats were seen to argue in favor of an expanded view of cerebellar function.

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TABLE OF CONTENTS

CHAPTER I

INTRODUCTION

The study of the cerebellum has traditionally been the domain of anatomists and physiologists. As a result of their efforts, a detailed picture of cerebellar fine structure and electrophysiology has emerged. Unfortunately, the emphasis in neurophysiological research has been placed largely on the role of the cerebellum in motor function. Psychologists, therefore, tend to be only marginally interested in this structure. A careful survey of the literature suggests, however, that the cerebellum may harbor functions which are of immediate interest to psychologists. Two principal lines of evidence will be presented to support the possibility of cerebellar participation in non-motor function. The first concerns evidence from the literature of "affective", autonomic, and EEG changes after cerebellar manipulation. The second presents direct experimental evidence of non-motor behavioral changes after cerebellar manipulation.

"Affective", Autonomic, and EEG Changes after Cerebellar Manipulation

"Affective" Changes

One of the earliest reports of affective changes after cerebellar manipulation was that of Pagano (1902). Pagano observed an apparent reaction of fear or anxiety in dogs after injection of 0.1 to 0.3 ml of 1% curare into the midline vermis. Reports of aversive reactions can also be found in studies using electrical stimulation. Clark (1939) noted that aversive reactions could be obtained after stimulation of the paramedian lobes in the cat. He further observed that cats frequently purred throughout the experiment; no indication was given whether this behavior was related to cerebellar stimulation.

A detailed description of aversive properties of cerebellar stimulation was provided by Chambers (1947). He showed that electrical stimulation of some cerebellar sites in cats resulted in forceful urination, marked pupillary dilation, piloerection, hypersensitivity to sound and touch, and attempted escape. Such reactions were most reliably obtained after stimulation of the medial vermis and the fastigial nuclei. Occasionally, cats attempted to bite their own paws and tails.

Chambers felt that the aversive reactions were not due to spread of current to extra-cerebellar sites since stimulation of points near the medulla and cerebrospinal fluid failed to give rise to affective responses. In addition, placements were found which, though equidistant from the brain stem, yielded entirely different responses with aversive reactions obtainable from one point but not the other, even though high currents were applied to the unresponsive site. Aversive reactions were also reported by McDonald (1953) after stimulation of sites near the fissura postcentralis in the cat. In connection with Clark's (1939) mention of purring during the experiment, the following quote from McDonald may be of interest: "Unless purring and so-called pleasure reactions commonly seen when the cerebellum was stimulated were part of a sensory effect the only responses noted in the present experiments were unpleasant ones" (McDonald, 1953, p. 80).

Stimulus bound affective behavior after cerebellar stimulation was also observed by Koella (1955). He noted that stimulation of the lingula and the brachium conjunctivum often resulted in licking and biting of the forelegs, hindlegs, anal regions, and tail. This behavior was accompanied by growling and meowing. In a number of cats, stimulation only elicited screaming without any motor behavior suggestive of a specific origin of an unpleasant sensation. Finally, Schoolman and Delgado

(1958) indicated that withdrawal reactions and salivation were observed after cerebellar stimulation but no particular details were given about the location of effective stimulation sites.

Changes in affective behavior have not only been observed after stimulation of the cerebellum but also after ablations in cats and as possible consequence of tumor development in children. Chambers and Sprague (1955) reported that ablation of the anterior lobe in a cat resulted in plaintive crying, panting, sweating, and wild, forced movements. While these symptoms describe the behavior of the animal immediately after surgery, constant kneading and purring was observed after the animal had recovered (17 days postoperatively). Lesions of the caudal third of the fastigial nuclei were reported to result in lethargy. In 1959, Sprague and Chambers suggested that cats with lesions of the entire vermis showed excessive friendliness and pleasure reactions and that "persistent pleasure reactions evinced by constant purring and kneading" could be observed after total cerebellectomies in adult cats. In addition, Sprague and Chambers claimed that cerebellectomized cats failed to organize escape or attack to painful stimuli.

The evaluation of possible changes in humans after cerebellar surgery is difficult because surgery here involves the removal of tumors. Thus, whatever changes may have taken place are likely to have taken place gradually

gradually and are therefore not amenable to analysis. The localization of tumors represents an additional problem since good autopsy material is rarely available and present knowledge does not permit localization of cerebellar tumors on the basis of clinical symptoms. Nevertheless, it may be of interest to consider a few pertinent observations of a correlational nature.

Davidoff (1945) reported on the behavior of 50 children with cerebellar tumors and came to the conclusion that they were characterized by "good cooperation, a high degree of intelligence and a sweet disposition" (Davidoff, 1945, p. 40). The "high intelligence" observed merits some comments. French (1948) published the results of psychological testing on ten patients who had undergone removal of cerebellar tumors during childhood. The intelligence of this group of children (average at testing was 8.1 years) was appreciably above the expected norm. Since relatively young children were described in both Davidoff's and French's studies, not too much weight should be given to the intelligence as defined by tests. Nevertheless, a high degree of cooperation is prerequisite to good test performance (Thompson, 1962) and the results, if nothing else, indicate that these children cooperated very well. In contrast to children with cerebellar tumors, children suffering from a so-called acute cerebellar syndrome (Blaw & Sheehan, 1958) tend to be alert but irritable. This syndrome

is usually of short duration and nothing is known about the pathology involved since patients invariably recover.

An entirely different type of cerebellar disturbance was described by Jervis (1950). Three young girls with severe cerebellar disfunction were found to be mentally retarded. In one case extensive degeneration of the granular layer and the Purkinje cells was observed. Jervis stated that "In the present case as in other cases of the literature the lesions found in the central nervous system outside the cerebellum were of little significance and insufficient to explain the severity of mental retardation" (Jervis, 1950, p. 406). Girard, Thevenin, and Lachanat (1951) suggested that when cerebellar anomalies occur in children, associated (unspecified) intellectual and character changes occur. It must be kept in mind, however, that extra-cerebellar brain anomalies may have been present but undetected in both studies. The problem of extra-cerebellar damage also makes it difficult to interprete the mental retardation observed in cases of complete cerebellar atrophy (Dow & Moruzzi, 1958).

Behavioral changes which are not in any obvious way related to motor function have been observed after cerebellar stimulation or lesions. The available evidence does not permit any meaningful statement as to location of effective stimulation, most effective stimulus para-

meters, or effects of localized lesions. Some thought should be given to the many studies in which non-motor behavioral changes were not recorded, and some explanations of why there was a failure to record such changes may be considered. First, non-motor behavioral changes may have been observed but not recorded because of their apparent incongruity. Second, such changes may emerge only under certain conditions which were not given in the majority of experiments. For instance, the observed aversive reactions may have been elicited only if the stimulation effects were superimposed upon an already existing background of strong excitation, or, in the case of ablations, the changes may have been apparent only to those who looked for them. Finally, affective changes may have been noted but were not recorded because they were deemed secondary to motor reactions.

Autonomic changes

It has been known for some time (Dow & Moruzzi, 1958) that stimulation of the cerebellum affects autonomic functions. Many of the older studies, particularly those concerned with changes in blood pressure after cerebellar stimulation, yield confusing and often contradictory results. In retrospect, it appears that many of the difficulties in these studies can be attributed to the use of inappropriate anaesthetics and failure to take into account the general condition of the prepa-

rations at the time of stimulation. For this reason, emphasis will be placed on more recent papers in which autonomic effects were clearly demonstrated.

Connor and German (1941) showed that vasomotor reactions were enhanced after ablation of the anterior lobe of the cerebellum in monkeys, dogs, and cats. Vasomotor reactions after stimulation of lobules V, VI, and VII of the cerebellum were obtained by Moruzzi (1947). Moruzzi's experiments were performed on acute thalamic cats which are known to exhibit high autonomic excitability. Cerebellar stimulation in these animals was also very effective in eliciting sham rage, of which the changes in vasomotor tonus may have been just one manifestation. Moruzzi noted that the kind of response following stimulation was a function of the background activity at the time of stimulation. If the cerebellum was stimulated during a quiet period, sham rage was produced. Conversely, if the cerebellum was stimulated during a spontaneous burst of sham rage, suppression of the sham rage occurred.

Zanchetti and Zoccolini (1954), also working with cats, corroborated Moruzzi's findings. Both studies indicate that elicited sham rage bursts were accompanied by sympathetic discharges (increase in arterial pressure, hyperpnoea, mydriasis, and retraction of the nictitating membrane). Zanchetti and Zoccolini showed that bursts of sham rage occurred both as result of stimu-

ation in the rostral and central fastigial nuclei and as rebound phenomenon when the posterior fastigial nuclei or portions of the tuber, pyramis, or uvula were stimulated. The autonomic and somatic sham rage effects were usually preceeded by the classical postural effects (Dow & Moruzzi, 1958) of fastigial stimulation. Sometimes, sham rage could be observed without these postural responses; in this case postural responses followed as a rebound effect. Zanchetti and Zoccolini felt that spread of current to extra-cerebellar sites was not likely to have produced the sham rage since electrocoagulation of an effective stimulus site abolished the response. They also stated that different autonomic responses could be obtained from sites which appeared to yield identical postural responses. This was seen to rule out involvement of a particular configuration of proprioceptive and tactile impulses in bringing about the sham rage. Zanchetti and Zoccolini speculated that the sham rage was indirectly produced by activation of the hypothalamus by way of fastigio-bulbar influences on the brain stem reticular formation. This argument was based on the fact that precollicular transections abolished sham rage responses after cerebellar stimulation even though such responses could still be observed after application of nociceptive stimuli. Ban, Inoue, Ozaki, and Kurotsu (1956) supported the speculation of hypothalamic involvement with the observation that hypotha-

lamic activity could be modified by repetitive cerebellar stimulation in the rabbit. Ban et al. (1956) also observed sympathetic manifestations after cerebellar stimulation. Certain problems of interpretation exist, however, since Ban et al. found cerebellar evoked responses more readily in the medial hypothalamus while it is the lateral hypothalamus which is involved in the expression of sham rage.

Further evidence of cerebellar-autonomic interaction was provided by Ban, Hilliard, and Sawyer (1960), and Sawyer, Hilliard, and Ban (1961). They showed that sympathetic discharges could be elicited in intact, anaesthetized rabbits by stimulation of the anterior cerebellar lobe. Such discharges consisted of a rise in arterial blood pressure (sinus bradycardia was often induced), mydriasis, exophthalmos, and cerebral EEG arousal patterns. While stimulation of the anterior lobe was consistently followed by sympathetic responses, a less consistent pattern was seen after stimulation of the posterior lobe. Often, posterior lobe stimulation brought about EEG desynchronization accompanied by pressor responses. Sometimes, however, EEG arousal was accompanied by depressor responses. Stimulation of the pyramis and uvula was, on occasion, followed by parasympathetic discharges (depressor responses, miosis, enophthalmos). A sympathetic rebound was usually observed. Of further interest is the fact that at one location a stimulus could produce a

sympathetic pattern at 8 V and a parasympathetic pattern at 3 V. Precollicular decerebrations or diencephalic lesions abolished the autonomic response to cerebellar stimulation while pressor responses could still be obtained at normal thresholds from brain stem stimulation. Sawyer et al. (1961) did not define the most effective stimulation sites in the posterior cerebellum but stated that in the anterior cerebellum sites near the fastigial nuclei in the culmen yielded the lowest thresholds. No indication was given whether stimulation of the fastigial nuclei gave similar effects to the stimulation in the white matter or cortex of the anterior cerebellum.

In interpreting their findings, Sawyer et al. suggested that the integrity of the hypothalamus and its connections with the cerebellum were essential to the production of autonomic responses after cerebellar stimulation. They stated that in the absence of the hypothalamus the connections of the fastigial nuclei were not sufficient to effect autonomic responses. Sawyer et al. proposed that the rostral third of the fastigial nuclei mediates sympathetic responses while the caudal two thirds mediate parasympathetic responses.

The findings of Yokoyama, Inoue, and Ban (1963) tend to support an anterior-posterior cerebellar differentiation in terms of autonomic responses in rabbits. They observed ergotropic responses (mydriasis, exophthalmos, rise in blood pressure, increase in muscle

tone, bladder relaxation, and EEG desynchronization) after stimulation of the anterior cerebellum and trophotropic responses (miosis, fall in blood pressure, contraction of bladder, and EEG synchronization) after stimulation of the posterior cerebellum. As in the experiments of Sawyer et al. (1961), however, Yokoyama et al. (1963) also observed mixed effects or pure ergotropic responses after posterior lobe stimulation. Hirai (1966) was not only able to show general sympathetic discharges after anterior cerebellar stimulation in cats but also showed that such stimulation resulted in an increased secretion of norepinephrine in two out of three cats.

The findings of Mitra and Snider (in preparation) suggest that the influence of the cerebellum on the autonomic system may, perhaps, be interpreted in terms of shifts of the ergotropic-trophotropic balance. They demonstrated that shifts of blood flow from the skeletal to the visceral musculature could be brought about by fastigial stimulation in the cat. There is some speculation that the effect was due to fastigial action upon the cardiovascular medullary reticular formation.

Cerebellar stimulation has been shown to affect autonomic function in cats and rabbits. The literature suggests that cerebellar influence on the autonomic sphere is not limited to isolated functions but seems to act through diffuse excitation of sympathetic and para-

sympathetic systems. While the relation between anterior cerebellar stimulation and sympathetic responses seems clearly established, no consistent relation has been found between posterior cerebellar stimulation and parasympathetic responses. The difficulty in establishing the latter relationship may partly be due to experimental procedures, i.e., preparations are usually well rested and show a parasympathetic tonus against which further parasympathetic changes due to stimulation cannot be easily detected. It is interesting to note, that postural rebound phenomena which are often observed after cerebellar stimulation find their counterpart in autonomic rebounds (Sawyer et al., 1961; Zanchetti & Zoccolini, 1954). This permits the interesting speculation that the cerebellum exerts its influence on the motor and autonomic spheres in similar ways.

EEG Changes

Some of the experiments presented in the previous section have shown that EEG changes may accompany sympathetic or parasympathetic discharges after cerebellar stimulation (e.g., Sawyer et al., 1961; Yokoyama et al., 1963). While such EEG changes are probably part of the general effects of cerebellar stimulation, they are of interest because some progress has been made in the localization of sites which affect EEG. In addition, some speculations on the nature of

cerebellar nuclear outflow are based on interpretation of EEG changes after cerebellar manipulation.

Following earlier work by Moruzzi and Magoun (1949) and Mollica, Moruzzi, and Naquet (1953), Fadiga, Manzoni, and Urbano (1966) provided a detailed study of the effects of cerebellar stimulation and lesions on the EEG activity in anaesthetized cats. Fadiga et al. (1966) noted that marked synchronization followed cerebellar ablations and traced this effect to the destruction of the inferior cerebellar peduncles. Since section of the brachium conjunctivum was ineffective, they speculated that the interrupted outflow of the fastigial nuclei to the brain stem via the inferior cerebellar peduncles was responsible for the synchronization. Closer investigation revealed a functional division in the fastigial nuclei: rostro-medial lesions brought about EEG desynchronization and rostro-lateral lesions brought about EEG synchronization. The finding of general EEG synchronization after cerebellectomy was supported by Fadiga, Manzoni, Sapienza, and Urbano (1968) who showed that similar effects could also be obtained by coagulation of the fastigial nuclei. Manzoni, Sapienza, and Urbano (1967), however, found that cooling of the fastigial nuclei produced behavioral and EEG arousal in unanaesthetized cats. This effect outlasted the cooling for several minutes. Manzoni et al. (1967) concluded that the fastigial nuclei normally exert a chronic

synchronizing effect on electrocortical activity. Such an interpretation stands in contradiction to the findings by Fadiga et al. (1966) and Fadiga et al. (1968) who showed that section of the inferior cerebellar peduncles or coagulation of the fastigial nuclei results in EEG synchronization in anaesthetized cats. Another problem with this interpretation is that the capacity of cerebellar stimulation to inhibit seizure activity in both hippocampus and cerebral cortex (Payan, Levine, & Strebel, 1966; Iwata & Snider, 1959) is not likely based on a synchronizing outflow from the cerebellum. The findings of Manzoni et al. (1967) could be explained if the cooling thermodes were not directly in the fastigial nuclei but in a location where corticonuclear fibers were cooled. This may actually have been the case.

There are some indications that the quest for the nature of the cerebellar influence on the electroencephalogram, as based on the consequences of cooling or lesions, may be quite naive. Fadiga et al. (1966) found that, at times, the predominant EEG activity after fastigial lesions would actually reverse. In addition, the EEG activity in response to cerebellar stimulation in unanaesthetized cats (Manzoni et al., 1968) and humans (Snider & Wetzel, 1965) was shown to be not only a function of the stimulus frequency and intensity but also a function of the EEG activity at the time of stim-

ulation. Thus, the influence of the cerebellum on EEG activity cannot be meaningfully described simply in terms of tonic synchronizing or desynchronizing effects.

Sawyer et al. (1961) indicated that stimulation of the anterior cerebellum tended to result in EEG activation while stimulation of the posterior cerebellum produced spindles similar to those seen when the rabbits were presumed to be in a sleepy state. The effects of posterior cerebellar stimulation, however, were not consistent; at times, desynchronization was observed.

At a given stimulus intensity, the effects of fastigial stimulation on the EEG depend on the frequency of stimulation. Low frequency (up to 15 Hz) stimulation tends to produce EEG synchronization in anaesthetized and unanaesthetized cats and high frequency (100-300 Hz) stimulation tends to produce EEG desynchronization (Fadiga et al., 1968; Manzoni et al., 1967). In unanaesthetized cats, low frequency stimulation can produce behavioral symptoms of drowsiness; such an effect is not unique to stimulation of the cerebellum (Pompeiano & Swett, 1962).

Stimulation and ablation of the cerebellum has clear influences on electrocortical activity. The important factors in determining the effects of cerebellar stimulation on EEG activity are stimulus frequency, stimulus intensity, type of preparation (unanaesthetized or

anaesthetized), location of the stimulating electrode, and type of EEG activity at the moment of stimulation. The most effective regions of the cerebellum in terms of effecting EEG changes are, as in the case of affective and autonomic changes, the medial vermal areas and the fastigial nuclei. The effects of cerebellar stimulation are not limited to cortical EEG; the electrical activity of the hippocampus can also be influenced (Iwata & Snider, 1959).

Some Aspects of Cerebellar Anatomy

Before an attempt is made to integrate the various lines of evidence on non-motor effects of cerebellar manipulation, a brief digression into some pertinent aspects of cerebellar anatomy may be of value. Emphasis will be placed on the anatomy of the cerebellar vermis since it is this region of the cerebellum which is most consistently associated with the responses under discussion. The cat cerebellum will be used for the discussion of cerebellar anatomy since most of the experimental work has been carried out on this species. Such species differences as may have relevance to the topic will be given particular consideration.

The following summary of functional cerebellar anatomy is based on the material contained in Elliot (1963), Everett (1965), Fox and Snider (1967), Larsell (1967), and Voogd (1964). Reference to specific research papers

will be made at appropriate points in the text.

External features- The surface of the cerebellum is marked by many gyri (folia) with intervening sulci and fissures which all extend in a transverse direction. The fissures occur with some constancy across individuals of a species as well as across species. They serve as landmarks for the division of the cerebellum into lobes and lobules. The cerebellum as a whole is divided into the lateral, paired hemispheres, and the medial, unpaired vermis. Beginning from the rostral and ventral position, the lobes which define the vermis (according to Larsell, 1967) are the lingula, central lobule, culmen, declive, folium and tuber, pyramis, uvula, and nodulus. Of these vermal lobules the nodulus is part of the phylogenetically oldest lobe of the cerebellum, the archicerebellum. The declive, folium and tuber are considered part of the neocerebellum which is thought to be functionally related to the cerebral hemispheres. The remaining lobules are part of the paleocerebellum which is thought to be functionally related to the spinal cord (spinal cerebellum). The declive, tuber and folium appear on the dorsal and medial aspect of the cerebellum. The divisions presented above are meant to serve as landmarks only. There is sufficient evidence to suggest that concise functional division of the cerebellum cannot be accomplished on the basis of lobules (Brodal, 1967; Voogd, 1964).

Afferent connections- The cerebellum receives a variety of inputs from almost all sensory modalities. Vestibular projections reach the cerebellum in the uvula, flocculus, and nodulus. Some fibers project directly to the cerebellum while others are relayed in the ipsilateral and descending vestibular nuclei. Vestibular fibers reach the cerebellum through the inferior cerebellar peduncle. Proprioceptive impulses from the lower extremities reach the pyramis, the uvula, and the vermis of the anterior lobe through the dorsal spinocerebellar tract. Proprioceptive impulses from all four extremities and the trunk reach the same vermal areas by means of the ventral spinocerebellar tract. The two spinocerebellar tracts differ in amount of crossover, details of projections and the type of afferent fibers they carry. Proprioceptive and tactile impulses from the neck, upper extremities, and the trunk reach the vermis and the regions interposed between vermis and hemispheres (intermediate zone) after relay in the lateral cuneate nucleus. Further proprioceptive information to the cerebellum derives from the medial and dorsal accessory olives. Olivocerebellar fibers do not appear to project to the dorsal midline region of the vermis (declive, folium and tuber).

Reticulo-cerebellar fibers reach the vermis from the lateral and paramedian reticular nuclei.

The dorsal midline regions of the vermis receive visual, auditory, and tactile (mainly from the face) information. Little is known about the pathways involved. Evoked responses can be recorded in the same cerebellar region after photic and auditory stimulation (Fadiga & Pupilli, 1964). One way in which the visual impulses may reach the cerebellum has been suggested by Altman and Carpenter (1961). They observed that a prominent bundle of tectopontine fibers passes caudally beneath the colliculi and terminates in the area of the dorsolateral pontine nuclei. These nuclei appear to project to the vermis (Brodal & Jansen, 1946). Generally, auditory evoked potentials show better localization than do visual evoked potentials. Auditory evoked potentials appear less well localized in fish, amphibians, and reptiles than in birds and mammals.

Cerebro-cerebellar projections seem to be mediated largely through the pontine nuclei. The cerebro-pontine-cerebellar afferent system is by far the largest of all afferent and efferent connections of the cerebellum (Tomasch, 1969). Speculations about cerebellar function frequently ignore this fact.

Some evidence is available on the sensitivity of the cerebellum to interoceptive stimulation from the stomach and the bladder. Firsov (1958) reported that the electrical activity of the vermis could be altered by distension of stomach and bladder. Following bilateral

vagotomy, the responses to stomach activity disappeared while responses to bladder distension were greatly diminished. In addition, there is evidence that the electrical activity of the cerebellum can be altered by vagal and olfactory impulses (Dow & Moruzzi, 1958).

Efferent projections- The functional division of the cerebellum has been based, in part, on efferent cortico-nuclear projection patterns. The lateral zone projects largely to the dentate nuclei while the intermediate zone projects largely to the interposed nuclei. The medial zone (vermis) projects almost exclusively to the fastigial nuclei. These projection patterns are relatively well defined in the cat but assume a more diffuse character in the rat. Goodman, Hallet, and Welch (1963) found that hemispheric lesions in the rat resulted in degeneration in all three nuclear groups, though clearly less in the medial than in the lateral nuclei. Vermal lesions resulted in heavy fastigial degeneration and lesser degeneration in the interposed nuclei. Of particular interest is a dorsolateral protuberance in the fastigial nuclei of the rat. Goodman et al. (1963) noted that this region seemed to be associated exclusively with the declive, tuber and folium as well as with all parts of the hemispheres with exception of the paraflocculi. They called this dorsolateral protuberance "neofastigial"; a similar region has so far not been identified in other mammals.

Goodman et al. also showed that a localized cortical lesion would result in degeneration throughout the longitudinal extent of the nucleus receiving fibers from that cortical zone. Degeneration in the cat appears somewhat more localized, i.e., a lesion in the anterior vermis will result in degeneration in the anterior parts of the cerebellar nuclei receiving fibers from that cortical area. The diffuse projection pattern in the rat might explain the fact that stimulation in a longitudinal zone in the rat will yield very similar motor responses, regardless of the particular lobule in which the electrode is located (Goodman & Simpson, 1961).

Even though the cortico-nuclear projection patterns in the cat are fairly discrete and can be considered within the concept of longitudinal projection zones on the basis of degeneration studies, a different picture emerges if the projections are investigated electrophysiologically. Deura (1969) found that if responses to cortical cerebellar stimulation in the nuclei are recorded, there emerges a very diffuse projection pattern. Cortico-nuclear projections, as assessed by this method, project fan-like in both the rostro-caudal and the medio-lateral planes.

Some interesting functional differences can be observed between the medial and lateral cerebellar zones if the distribution of evoked potentials on the cerebral

hemispheres after stimulation of these zones is considered. The lateral and intermediate zones are characterized by fairly well localized and largely contralateral influences on cerebral activity. The anatomical pathways which might underlie these responses are not well understood. There is some suggestion that the ascending connections of the nucleus ruber, which receives projections from the lateral cerebellar nuclei might be involved (Evarts & Thach, 1969) but it should be recalled that the nucleus ruber does not appear to have noticeable ascending connections in man and monkey. In contrast to the lateral cerebellar zones, the vermis exerts its influence on cerebral activity in a diffuse and bilateral way. Because of the diffuse and bilateral influence, it might be suggested that the vermis exerts its ascending influences via the reticular formations of di- and mesencephalon. The fastigial nuclei can influence the brainstem reticular formation through two pathways. First, there is the direct fastigio-bulbar tract which, originating mainly from the rostral part of the nuclei, projects to the central part of the reticular formation. This tract projects stronger ipsilaterally (but bilateral activation might come about through the extensive commissural connections between the fastigial nuclei). Second, there is the contribution of the caudal fastigial nuclei to the ascending branch of the uncinate fasciculus. The fibers in this tract project contralaterally and ascend around

the dorsomedial pole of the brachium conjunctivum to terminate in both the di- and mesencephalon; a large number of fibers seem to terminate in the thalamic intralaminar nuclei (Voogd, 1964).

A review on electrophysiological data pertaining to the diffuse projections of the cerebellar vermis to many regions of the brain was provided recently by Evarts and Thach (1969).

The cerebellum, rather than being only related to spinal motor centers, has extensive connections with the cerebrum and the reticular formations of the di- and mesencephalon. The vermis in particular receives teleceptive, exteroceptive, and interoceptive information.

Discussion

A review of "affective" changes after cerebellar stimulation or ablation meets with a number of severe difficulties. Observations made on "affective" changes after cerebellar manipulation often seem incidental and there is sometimes no guarantee that the changes are directly related to cerebellar function. Furthermore, and particularly in the older studies, little information is given about stimulation parameters and lesion extent. Speculations about the nature of cerebellar involvement in non-motor behavioral changes must therefore be approached with caution.

One possible explanation of aversive reactions after cerebellar stimulation lies in observations made by Fangel and Kaada (1960). They found that behavioral arousal could be elicited by stimulation of some cerebral cortical areas in the cat. Increase of stimulation intensity in some of these sites resulted in cringing, slow withdrawal, and flight. Related observations were made by Segundo, Arana, and French (1955) in the monkey. Thus, the aversive responses after cerebellar stimulation may simply represent the extreme of an arousal response. Such an explanation, however, could not easily account for the purring (Clark, 1939; McDonald, 1953) or the paw and tail biting (Chambers, 1947; Koella, 1955) seen af-

ter cerebellar stimulation. These latter observations might argue for the presence of somatic sensations in some cases of cerebellar stimulation. In this context, the failure of human subjects to report conscious sensations or sensory losses after cerebellar stimulation (Snider & Wetzel, 1965) may be of interest. Experiments on humans are limited, however, by the fact that high stimulation intensities cannot be used. Snider and Wetzel's patients were aware of the fact that they were stimulated and may not have registered a non-specific feeling of arousal because of general tension. Schachter and Singer (1962), on the basis of injecting human subjects with epinephrine, have concluded that given a state of physiological arousal for which an individual has no immediate explanation, he will label this state in terms of the cognitions available to him. Thus, the human patients of Snider and Wetzel may have actually felt some non-specific arousal which was, however, not amenable to identification because of the experimental conditions. Circumstantial evidence that somatic sensations might have some importance after cerebellar stimulation derives from Chamber's (1947) observation of hypersensitivity to sound and touch in cats after vermal stimulation and the fact that the pain threshold is raised in cats after cerebellectomies (Sprague & Chambers, 1959) and in humans after occlusion of the superior cerebellar artery.

As far as the behavioral changes after cerebellar lesions in cats and tumor development in children is concerned, the possibilities for a meaningful analysis are even dimmer. It might be suggested that the behavioral changes are secondary to motor deficits. There is actually little to suggest that the motor deficits in children with cerebellar tumors were very severe (Davidoff, 1945). In the case of cats (Sprague & Chambers, 1959) the possibility remains open. It would have to be shown that cats with motor deficits generally undergo such changes as were observed. It is quite obvious at this point that only careful observation of non-motor behavior in animals and humans after cerebellar lesions and stimulation can clarify the situation.

The relation between cerebellar stimulation and autonomic responses is somewhat clearer. Generally, the effects of cerebellar stimulation can be described in terms of diffuse activation of sympathetic and parasympathetic systems. It has been pointed out previously that some differences exist between the activation of these systems by cerebellar stimulation. One possible explanation is that the type of preparation used is more apt to show sympathetic than parasympathetic responses. Alternatively, the differences may reflect the individual properties of the two systems. That is, the sympathetic division of the nervous system has been evolved to respond quickly to stimulation while parasympathetic

activity may generally only appear when sympathetic activity subsides and is a passively occurring, rather than an actively induced, activity.

Even though past experimentation argues largely for a generalized influence of the cerebellum on the autonomic system, there is some evidence that this influence is exerted over some surprisingly direct and specific pathways. Miura and Reis (1969) showed that low intensity stimulation of a very small region in the rostral ventromedial fastigial nucleus produces very large blood pressure responses. The fibers which mediate this response apparently project from this fastigial region to the paramedian reticular nucleus (which receives input from the carotid sinus nerve).

How important is the cerebellar influence on autonomic activity in terms of the normal functioning of an intact organism? The question is difficult to answer but there is evidence that the cerebellar influence may be of appreciable importance. Chambers and Sprague (1955) observed that cats with ablations of the anterior cerebellar lobe showed sweating and panting, and Connor and German (1941) showed that vasomotor reactions were enhanced after ablations of the anterior cerebellar lobe in monkeys, dogs, and cats. A promising approach to the problem has been taken by Ramu and Bergmann (1967). They studied the responses of the circulatory system to

peripheral (sciatic nerve) stimulation before and after lesions of the cerebellum in anaesthetized rabbits. Total cerebellectomies completely reversed the usual increases in blood pressure after peripheral stimulation and only decreases could be observed. Ramu and Bergman also noted that prominent and intensified Mayer waves, which persisted until death, could be seen after ablation of the vermis.

There also exist questions about the relative importance of cerebellar influences on EEG activity in the cerebral cortex. Little has been done which could help to answer this question. Future research could perhaps concentrate on possible EEG changes after cerebellar ablations or investigate possible differences in EEG activation after such ablations.

Conclusion

The preceding review suggests very clearly that the role of the cerebellum is not restricted to functions in the motor sphere. Both the autonomic and the EEG changes after cerebellar manipulation indicate ascending cerebellar influences. Could it be that the "affective" changes observed after cerebellar stimulation and ablation are also a manifestation of ascending cerebellar influences? In the absence of any conceptual framework within which to approach the problem, the following hypothesis will be used to guide further thought.

One likely function of the cerebellum is that it participates in the maintenance of background levels of activity in the motor systems. The maintenance of such background activity is a highly complex task because it requires integration of information concerned with exteroceptive, teleceptive, interoceptive, and cognitive (anticipation of movement) factors. Only if the background levels of activity in the motor system are in correspondence with the ongoing activity in the organism can voluntary and reflexive movements be executed smoothly and efficiently. Just as the background activity in the motor system is important for the efficient performance of movement, the background activity in the primary sensory areas of the cortex is essential for the efficient reception of sensory stimuli. That is, in order to operate efficiently, the sensitivity in sensory cortical areas must be in correspondence with the general state of excitation of an organism. Snider (1967) has provided evidence which allows for the possibility that the cerebellum influences not only motor but also sensory tonus.

The analogy can be extended one step further. In order for an organism to operate efficiently, its background levels of autonomic activity must be in correspondence with the general state of excitation. This also applies to the background levels of activity in systems concerned with the elaboration of emotion and motivation.

It is proposed that the cerebellum participates not only in the regulation of motor and sensory tonus but also in the regulation of autonomic (and, perhaps, emotional) tonus. If the above hypothesis is useful, it should be possible to demonstrate that animals with cerebellar lesions differ from normal animals in their response to conditions involving emotional and autonomic arousal. Indirect and circumstantial evidence that this may be the case has been discussed, but there has been only one pertinent experimental approach (see p. 4) to the problem (Sprague & Chambers, 1959). The following sections will present attempts to substantiate Sprague and Chambers' (1959) findings. In addition, different approaches aimed at the much needed investigation of overt non-motor behavioral changes after cerebellar manipulation will be presented.

CHAPTER II

EXPERIMENT 1

The only direct experimental evidence on "affective" changes after cerebellar ablations was reported by Chambers and Sprague (1955), and by Sprague and Chambers (1959). They indicated that cats with vermal lesions or total cerebellectomies were noticeably friendly and showed strong pleasure reactions. Unfortunately, it was not specified whether these behaviors emerged only in interaction with the experimenter or also with other cats. This point is of some importance since the motor deficits resulting from cerebellar injury may bring about a loss in dominance which in turn may affect the response of animals to the experimenter and other cats. Furthermore, in order to assess postoperative changes, some knowledge of the preoperative "personality" of the animals is essential. Such a knowledge, in all likelihood, was lacking in the above studies. Because of the potential value of Chambers' and Sprague's observations, an attempt to confirm their data seemed desirable.

Most of the cats available for this experiment were moderately friendly to begin with (towards the experimenter but not necessarily towards other cats). This resulted in a certain difficulty in terms of establishing a baseline against which postoperative changes could be measured. To avoid this problem, at least to some extent, and to provide some generality to the findings, a number of squirrel monkeys (Saimiri sciureus) were also subjected to cerebellar lesions. The squirrel monkeys had been caught in the wild and were untamed and unhandled by laboratory personnel.

The limitations of a purely observational study without quantification of the observations are obvious. This study of "affective" changes, therefore, was carried out to determine whether the changes were marked enough to warrant further investigation rather than to provide a detailed analysis of the changes.

Method

Subjects- Three male and three female adult domestic short-haired cats of unknown background and three kittens (two male, one female), born in the laboratory colony, were used. In addition, four young adult male squirrel monkeys, purchased from a dealer, were used.

Procedure- All adult cats were observed in interaction with the experimenter and other cats for at least four weeks preoperatively. The cats were housed individually during the night and in mixed groups of about eight animals in a 1.90

by 1.70 m enclosure during the day. Water and cat chow were available ad libitum in both situations. With respect to cat - experimenter interaction, the ease of handling, response to stroking and petting, and the tendency to approach and follow the experimenter were recorded before and after surgery. The assessment of interactions among cats involved observation of dominance relationships. In females, dominance was assessed by noting whether a female would retreat or attack if another female approached and which of two females had priority during feeding. In males, dominance was assessed by noting which male retreated or challenged during confrontations and which male had priority during feeding. The postoperative survival time for cats was at least two months and at most 1.5 years.

Preoperatively, the monkeys were untamed and could not be handled. A dominance order among the monkeys could not be clearly observed. This might be related to the fact that the animals had not been in the colony for long and that no females were present. Postoperatively, the reaction of monkeys to physical contact with the experimenter was recorded. The minimum survival time for the monkeys was two weeks with a maximum of three months.

Average daily observation time was roughly 30 min for cats and 30 min for monkeys over four weeks before and four weeks after surgery. Thereafter, the animals were observed several times a week for a similar length of time. Experimental and control animals were observed together.

Surgery- Three total cerebellectomies were performed on kittens not older than 36 hours. A combination of ether, local cooling, and procaine hydrochloride was used to anaesthetize the subjects. Three adult cats and four squirrel monkeys received ablations of the folium and tuber region (removal of this region appeared to produce the effects described by Sprague and Chambers). Three adult cats were subjected to sham-operations. In two of these the dura overlying the folium and tuber vermis was cut while in the third a small portion of the paramedian cortex was removed unilaterally. Surgery was performed under deep sodium pentobarbital (40 mg/kg, i.v. in cats, and i.p. in monkeys) anaesthesia and semisterile (cats) and aseptic (monkeys) conditions. All ablations were performed by aspiration. Adult cats received penicillin for three days after surgery.

Results

Histology- All animals were perfused with normal saline and 10% formalin. In cats 4, 17, and 32 the tuber and folium of the vermis were severely damaged; the damage extended to the pyramis in cats 4 and 32. Kitten 27 had undergone a complete cerebellectomy while in kittens 26 and 50 the cerebellectomy was almost complete.

In monkeys 1 and 4 the tuber and folium vermis had been damaged severely while in monkey 3 the damage extended into the deep portion of the cerebellum with probable damage to the posterior aspects of the cerebellar nu-

clei. Monkey 2 sustained the smallest lesion and the tuber and folium in this animal were largely undamaged.

Representative illustrations of posterior vermal ablations in cats and monkeys and a cerebellectomy are presented in Figures 1, 2, and 3.

Motor Deficits and Related Observations

Cats with vermal lesions- The three cats with vermal lesions had severe difficulties in jumping for at least two weeks postoperatively. Most commonly, they would overshoot their aim and often, when attempting to jump on a table, they would jump straight into the air and fall back down. If they managed to reach the table, they had a tendency to fall over backwards (this was particularly marked in cat 32). This tendency may be related to damage to the pyramis since similar observations have been made in dogs and rabbits after pyramis destruction (Dow & Moruzzi, 1958). When jumping on a table, the animals often touched with their hindlegs first, which stands in contrast to the behavior of normal cats which tend to lightly touch with their forelegs before landing on their hindlegs. The difficulties in jumping were not in any obvious way related to muscle weakness but appeared to be due to an inability to correctly integrate a distance judgement with the amount of force required to traverse that distance. While the animals eventually improved their jumping, they did not learn to jump as efficiently and smoothly as normal cats within their survival period. Immediately after surgery

the cats showed a marked impairment in their hindlegs (particularly cat 32); these were placed in an unsteady manner during walking and gave the cats a wide-stanced gait. The abnormality in gait was very obvious in cat 32 and could be seen throughout its survival period. Any deficits in the use of forelegs were not obvious to casual observation.

None of the subjects had the ability to orient briskly and smoothly to auditory stimuli. The fast, often independent, orienting movements of the external auditory pinnae, as seen in normal animals, were not observed. Fast and smooth visual tracking was also absent. A mild head tremor during visual tracking, in addition to a slight horizontal nystagmus was observed in cat 17. These symptoms were not evident in cats 4 and 32. Superficial observation of the subjects suggested that they showed somewhat less spontaneous movement than normal animals. This may have been largely due to damage posterior to the tuber and folium because animal 17, in which damage did not extend very far into the pyramis, was fairly active. During fights, these animals seemed to be able to strike with adequate speed and accuracy. It is quite possible, however, that more thorough testing with help of motion pictures would reveal a deficit here.

Sham-operated cats- No obvious changes could be detected in the motor behavior of cats 6, 15, and 18.

Cerebellectomized kittens- Similar to cerebellectom-

ized adult cats, the cerebellectomized kittens developed a hypertonus of the extensors which became obvious as soon as they could walk. Unlike the cats described by Sprague and Chambers (1959), these animals showed no poverty of voluntary movement and were quite active. A tendency to tire was noted but this was attributed to the relatively large effort needed to move about. Subjects 26 and 50 learned to walk without lateral support but they were not able to run or walk straight ahead in a coordinated manner. Instead, they advanced in an oblique forward approach with severe staggering and swaying. Marked goose-stepping was observed in the forelegs during walking. Subject 27 could walk in a very impaired fashion at the time of weaning but could not walk without lateral support at a later age and did not learn to do so within the postoperative survival period of one year. At one time, cat 27 was seen to run in an uncoordinated fashion for about 4 meters in an attempt to catch a butterfly. This was but one demonstration of the fact that the animal could show visual tracking. None of the animals showed any obvious nystagmus or chronic pupillary dilation.

Orientation to sudden loud noises was absent or poor but the kittens did orient to rattling of food dishes or to food calls. As in the case of cats with vermal lesions fast orienting movements of the external auditory pinnae were absent.

All kittens nursed successfully and, after weaning,

ate voluntarily and without help. They were voracious eaters and consumed large quantities of food at a time. Subject 27 showed strongly competitive behavior while feeding (growling, flattening of ears) with its unoperated littermates. When feeding, the kittens showed a very coarse tremor which resembled a pecking motion. The passing of urine did not seem to present any obvious difficulty, in contrast to observations made by Sprague and Chambers (1959) on adult animals.

Species specific behaviors appeared well developed in all three kittens. They learned to groom themselves adequately (in kitten 27 proper grooming only appeared at about 6 months of age); grooming behavior usually developed after the kittens began to lick their forepaws. Vocalization seemed to be normal and growling, hissing, attention-seeking meowing, and purring were observed. During fights, the kittens defended themselves within the limits of their motor capacities and ear-flattening and hissing was observed. All animals showed play-hunting behavior and could bat a paper ball with surprising speed and accuracy if they were held so that they did not need their limbs for support.

The kittens appeared well muscled and seemed to be in good general health. Sexual behavior, both directed towards or by the kittens was not observed.

Monkeys with vermal lesions- Monkey 3 appeared severely paralyzed and had limited use of its left hand only. There

was no improvement over the postoperative survival period of 2.5 weeks. Monkeys 1 and 4, and, to a lesser extent, monkey 2 showed difficulties in jumping. At times, monkeys 1 and 4 would jump straight into the air, and if they reached the wire mesh of their cage they often failed to grasp it properly and fell back to the ground. After a few intitial attempts, the animals would generally cease jumping until two or three weeks had passed. After that time they showed very little spontaneous jumping and, if jumps were executed, they tended to be stereotyped in the sense that they started and ended in the same place. Superficially observed, the monkeys seemed to show less spontaneous movement than normal animals; this tendency was most marked in animal 1. The animals never seemed to be able to run or climb as fast as normal animals and were not seen to walk on a rope which was strung across the enclosure, as they did preoperatively. During climbing a slight hesitancy in placing and grasping could be detected by very careful observation.

Subjects 1 and 4 showed a lack of brisk orientation to sudden loud noises while subject 3 appeared to orient adequately. Thus, the deficits in orienting may be specifically due to damage of the tuber and folium vermis.

Monkey 3 showed the same kind of pecking motion during feeding as was observed in the cerebellectomized kittens.

Affective Changes and Related Observations

Cats with vermal lesions- Subjects 4, 17, and 32 were more amenable to handling by the experimenter than before surgery. They showed strong pleasure reactions to stroking (marked kneading, purring, and head rubbing) and tended to seek out the experimenter. Subjects 17 and 32 developed a tendency to follow the experimenter through the laboratory if they were permitted to leave the enclosure. All three cats appeared definitely more "friendly" towards the experimenter after surgery. All three animals engaged in sexual behavior. Both cats 4 and 17 conceived and gave birth postoperatively.

Cat 32 had been the dominant male in the colony before surgery and he retained his status postoperatively. This animal was challenged on a number of occasions and seemed to possess fighting ability sufficient to retain his dominance. Cat 4, a high ranking female, also retained her status postoperatively. No changes were observed in cat 17, a neutral to low-ranking female.

Sham-operated cats- No changes could be detected in these animals.

Cerebellectomized kittens- All three animals were very responsive to stroking and general handling. They showed marked pleasure responses (kneading, purring, and head rubbing) to stroking and petting. These reactions were noticeably stronger than those observed in their unoperated littermates. Kittens 26 and 50 developed a

tendency to follow the experimenter through the laboratory if permitted to leave their enclosure. Normal subjects did not show such pronounced following behavior. The kittens were generally well tolerated by normal, adult cats. At the age of about 2 months the kittens had to be protected from a few vicious attacks by some older animals but such incidences did not occur after that time. Usually, the kittens were ignored by the older animals.

Monkeys with vermal lesions- Monkeys 1 and 4 permitted the experimenter to touch and stroke them throughout their postoperative survival period. This was in dramatic contrast to their preoperative shyness. The animals did not show any particular signs of excitement when approached which was also in contrast to the behavior of monkeys 2 and 3. Monkey 2 was fearful and attempted escape whenever attempts of handling were made and monkey 3 showed signs of strong agitation if it was touched (shrieking, attempting to bite). A very surprising observation was that subjects 1 and 4 showed very little vocalization within their postoperative survival period; monkey 1 would only produce a series of dry clicking sounds and none of the usual varied sounds heard in squirrel monkeys.

Discussion

Sprague and Chambers' (1959) statement, that cats with vermal lesions and cerebellectomized cats show marked pleasure reactions and "friendliness", was supported.

The friendliness did not in any obvious way extend to interactions with other cats and can therefore not be attributed entirely to a general placidity and docility. The most obvious aspect of the behavioral changes was the enhanced reactivity of animals to stroking and petting. Such changes were not brought about by the general surgical procedure and postoperative care, as is illustrated by the sham-operated control subjects. In the case of the cerebellectomized kittens the tendency to seek out the experimenter may have been related to the need for lateral support. However, such a support could have been secured from inanimate objects.

One factor which could possibly account for the "affective" changes is the amount of attention paid to the animals postoperatively. While an attempt was made to direct attention equally to control and experimental subjects, this possibility cannot be entirely discounted. Nevertheless, in the monkeys the differences appeared very soon after surgery; monkey 2 could not be handled one day after surgery which makes the factor of attention irrelevant in this case. Monkey 3 could not escape handling but did not become accustomed to contact with the experimenter. In this case even intense attention did not bring about any changes in the direction of greater tractability.

A certain poverty of auditory and visual attention was noted in all subjects with damaged tuber and folium vermis or cerebellectomies. The term "poverty of attention"

may be somewhat unfortunate since it must be qualified. All animals, including the cerebellectomized kittens, would orient to meaningful noises such as rattling of the food dishes, food calls, or calling of their names. That the animals were capable of paying attention to fairly subtle visual and auditory cues is illustrated by the following fact. Cats 4, 17, and 32 were trained in a task which required visual and auditory attention as well as an instrumental response in order to obtain a food reward. In a Skinner - type box, a lighted bulb would signal to the animal that a center lever could be pressed which in turn would activate a loudspeaker over either of two levers. If the animal pressed the lever which was associated with the sound, it would receive a food reward. The animals were also capable of performing a discrimination between two simultaneously presented clicks of different repetition rates. Cats 4, 17 and 32 performed these tasks as well as unoperated control animals (A. Monjan & M. Peters, unpublished work). This suggests that neither attention as such nor orientation was lacking in these anmals. In addition, Munson and Monjan (1967) demonstrated that no losses in auditory threshold could be found in cats with lesions of the folium and tuber vermis. A poverty of visual and auditory attention, as observed in this study, however, was reported by Chambers and Sprague (1955) in a cat in which the tuber and folium vermis had been destroyed. Rademaker (1931) made some observations on the auditory attentiveness of cerebellectomized dogs which may best

describe the puzzling facts presented above. He noted that cerebellectomized dogs failed to orient to incidental noises even though they would orient to meaningful ones (e.g. food whistle). Thus, there seems to be a dissociation in attentiveness to incidental and meaningful noises after cerebellectomies or destruction of the folium and tuber vermis.

A number of studies on the effects of posterior lobe lesions in dogs and monkeys (Keller, Roy & Chase, 1937) and cats (Sprague & Chambers, 1955) state that only very transient motor deficits follow such lesions. In the present study, subtle deficits in jumping and rapid locomotion were observed in both cats and monkeys for the entire period of survival. If nothing else, this difference proves the shortcoming of simple observations for purposes of scientific communication. It is suggested that the use of formalized testing procedures may both aid in the analysis of motor deficits after restricted vermal ablations and improve meaningful communication of the findings.

Conclusion

The demonstration of "friendliness" after vermal lesions in cats and monkeys does not, in itself, yield any information about the origins of this friendliness. An attempt must therefore be made, to break down the phenomenon into component factors. A clue about the direction such an analysis could take is provided by the fact

that cats with vermal lesions were strongly reactive to stroking and petting. Using this information, the problem could be approached with the general question: are the affective changes largely a result of the increased reactivity of animals to certain reinforcers? Such a question can be attacked experimentally. The following series of experiments was designed to investigate whether vermal lesions change the reactivity of animals to reinforcers. Rats were used as experimental animals since this permitted control of variables such as age, heredity, and background experience. In addition, the rats were tested in a way which permitted quantification of the dependent variable which improved the chances of drawing meaningful distinctions between experimental and control groups.

CHAPTER III

EXPERIMENT 2

Experiment 2 was designed to study further the nature of behavioral changes after vermal lesions. Since the cats in Experiment 1 showed a strong response to stroking, the working hypothesis that vermal lesions change the reactivity to reinforcers was adopted. To test the usefulness of this hypothesis, rats with vermal lesions were trained and tested in tasks involving responses to conventional reinforcers (food, electrical shock). The performance of rats with vermal lesions on these tasks was compared to that of sham-operated rats.

Experiment 2 a, Food Approach

Method

Subjects- Twenty male Montreal Black-Hooded rats, averaging 250 gm, were used. The animals were obtained from the Collip Laboratories at the University of Western Ontario.

Apparatus- A 10 by 150 cm grid-floored straight alley, painted flat grey, with 30 cm walls was used. The alley had a 18 cm start section, which was separated from the runway by a guillotine door, and a 28 cm goal section. The goal section was not distinct from the runway other than that its grid could be electrified by a high resistance shocking device. A concave, semicircular metal food cup was attached 1.6 cm above the grid floor and 3.8 cm from the end wall of the goal section. Running latencies were measured with a Meylan timer which was triggered and stopped by two photocells. The first photocell was attached 1.2 cm outside the start section and the second 1.2 cm in front of the food cup. Both photocells were located 1.8 cm above the grid floor. Interruption of the first photobeam started the timer and interruption of the second stopped it.

Procedure- Ten Ss received ablations of the dorsal vermis (experimental group) and in ten Ss a groove was drilled into the bone overlying the vermis (control group). Surgery was performed under deep sodium pentobarbital anaesthesia (60 mg/kg, i.p.). After a recovery period of ten days all Ss were placed on a 24 hr food deprivation schedule. Subjects were housed in pairs.

On Days 11 to 13, each S was given a daily exploration period of 20 min in the alley. During these periods the guillotine door was removed and the food cup was filled with 45 mg food pellets.

On Day 14 training commenced. Subjects were placed in the start section of the alley and the guillotine door was raised. The time taken to reach the food cup was used as the dependent variable. Failure to reach the food cup within 120 sec resulted in the termination of a trial. Subjects were given five trials daily for ten days; the median latency of the five trials was used as performance measure. Two 45 mg food pellets per trial served as food reward. After the daily training period Ss received wet mash ad libitum for one hour.

Results

Inspection of Figure 4 indicates that the experimental animals approached the food cup sooner than the control animals on the first five days while the reverse was seen on the second five days. For this reason, the first and second five days of training were analyzed separately. The median latencies (Table 1) suggest marked differences in variability between the groups which made it necessary to test for group differences with a non-parametric test. A Kruskal-Wallis non-parametric analysis of variance (Siegel, 1956) showed that on the first five days of running the experimental Ss reached the food cup significantly sooner ($H = 3.86$, $p < 0.05$) than the control subjects. On the second five days the control Ss reached the food cup significantly sooner ($H = 9.14$, $p < 0.05$) than the experimental subjects. The last difference reflects, in all likelihood, the differences in motor

ability between the two groups; subjects with vermal lesions could simply not run as fast as sham-operated subjects.

Experiment 2 b, Passive Shock Avoidance

Method

Both the Ss and apparatus were the same as in the preceding experiment. On Day 24, experimental and control groups were divided into subgroups of five animals. Training procedures on Day 24 were the same as those used on previous days with the exception that the Ss, upon reaching the food cup, received a 1 sec electrical shock. Five Ss of each group received a 0.4 mA shock while the remaining Ss received a 0.8 mA shock. Failure to approach the food cup within 120 sec over five consecutive trials was counted as successful avoidance. Subjects were run under this condition for a maximum of seven days.

Results

Figure 5 shows that the experimental Ss avoided the shock sooner than control Ss under both low (0.4 mA) and high (0.8 mA) shock conditions; the difference is somewhat more marked under the high shock condition.

Experiment 2 c, Active Shock Avoidance

Method

Subjects- Eighteen of the Ss from the preceding experiments were used.

Apparatus- An 18 by 35 cm grid-floored shuttle box with 20 cm walls was used. The two halves of the box were separated by a removable partition which had a center opening 7 cm wide and 10 cm high at its bottom. One compartment of the box was painted glossy white and the other glossy black. A lid prevented escape from the box. The grid of the box could be electrified by a high resistance shocking device. A Foringer model 1925 Grid Shock Scrambler served to scramble the shock. The two compartments of the box could be electrified independently; a shock level of 0.4 mA was used throughout the experiment.

Procedure- The subjects were housed in pairs and were given food and water ad libitum. Subjects were first trained to avoid shock by escaping into the black compartment within 5 sec of having been placed into the white compartment. They were always placed into the compartment so that they faced a rear wall corner of the shuttlebox. Subjects were given three trials daily for eight days. The time taken from placement into the white compartment to escape into the black compartment, measured by stop watch, was used as dependent variable. The median latency of the three daily trials was used as performance measure. On Day 9, Ss were placed into the black compartment where they had to avoid shock by escaping into the white compartment within 5 sec (first reversal). Subjects were run under this condition for eight days, with three

trials per day. After 16 days of training, the motor performance of the two groups was considered comparable and the third training session commenced.

Following the last trial of Day 16, each S received three 10 sec shocks within 1 min in the black compartment of the shuttle box. During this time a solid partition prevented escape. The shocks served to ensure that Ss would remain in the white compartment until shocked at the beginning of training. Training followed the procedure used during the preceding 16 days; subjects had to esacpe into the black compartment within 5 sec of having been placed into the white compartment (second reversal). Three daily trials were given for eight days under this condition.

Results

During the first eight days of training experimental Ss avoided somewhat more slowly than control subjects (Table 2). Although the difference was not significant, experimental subjects seemed to turn clumsily and any difference in latencies was attributed to this factor. Figure 6 a shows that during the second eight days of training (first reversal) the performance of the groups seemed well matched (the median latencies are presented in Table 3). Clearly, the training procedure was not sensitive enough to show any differences between the two groups. Under the third condition (second reversal), however, the Ss had to escape into a compartment in which

they had been shocked without possibility of escape and from which they had to escape during the first reversal. The response of the Ss depended therefore both on their reluctance to enter the black compartment and the immediate effect of shock in the white compartment. Figure 6 b shows that experimental Ss avoided sooner ($t = 2.78$, $p < 0.05$) than control subjects (see Table 4 for the median latencies).

Activity Measures and Food and Water Intake

All animals were given a 10 min activity test in a 120 by 120 cm open field with 30 cm walls 32 days after surgery. The open field was divided into 16 equal squares and the number of squares crossed within 10 min was recorded for each animal. The open field performance of experimental and control groups did not differ significantly (Table 5). Nevertheless, tests on additional groups of animals, four days after surgery, again indicated that animals with vermal lesions have a somewhat lower group mean of crossed squares (Table 6).

A comparison of activity wheel performance also failed to differentiate between the two groups (Table 7). The same negative findings apply to a "time taken to leave the cage" test. In this test the home cage of the animal is pulled out of the rack one third of its length and the time taken by the animal to leave the

cage is recorded. While all of the Ss with vermal lesions left their cages within the given period of 30 min, three of the control subjects failed to do so (Table 8).

Measures of food and water intake did not reveal any differences between the two groups on a statistical basis. However, pilot studies on different groups of animals suggest that animals with vermal lesions tend to have a slightly lower mean daily water intake than normal animals.

Histology

All animals were perfused with 10% formalin and normal saline. The brains appeared to be in good condition and no obvious infections, hematomas, or other abnormalities were noted. The ablations were found to be fairly uniform and the tuber and folium vermis had been removed in all animals. The lesions generally extended from sublobules a and b of the declive to the pyramis. Since the superior cerebellar veins were used as lateral limits of the ablations, there was rarely any damage beyond the intermediate longitudinal zone of the cerebellum. An illustration of lesions representative in surface extent, depth, and general location is given in Figure 7.

The brains were sectioned in the transverse plane by the frozen method and the sections were stained with a cresyl violet Nissl stain. Inspection of the sections indicated that, with possible exception of animals 6 and

10, there was no direct damage to the cerebellar nuclei. In Ss 6 and 10 there might have been some very slight infringement upon the superficial aspects of the fastigial nuclei.

Discussion

The first question to be considered is: are there any obvious motor deficits after vermal lesions in rats and could these account for the performances of the experimental and control groups? Motor deficits in the rat are difficult to establish because "normal" motor behavior is not easily defined in this species. Nevertheless, a few disturbances were noticed during the first post-operative week. The animals walked with a slightly tumbling gait and showed hesitant placing of the hind-legs. The animals seemed to show adequate orientation to sudden noises; abnormalities may have existed but were not obvious to casual observation. Sometimes a slight tremor was observed in animals 6 and 10 up to two days after surgery. This tremor was seen quite clearly during head movements. All obvious motor deficits had disappeared at about one week after surgery. That motor deficits were still present after this time is indicated by the slower running times shown by the experimental subjects on the second five days of the Food Approach task and the clumsy turning of animals with vermal lesions during training in the shuttlebox.

Of particular interest with view to the observations made in Experiment 1 was the fact that two subjects jumped clear over the wall of the open field during an activity test (Ss 1 and 6). If normal rats develop a jumping habit in the open field, they invariably jump to the edge of the wall and from there on down to the other side. It is quite possible that careful investigation would reveal jumping deficits in rats.

While motor deficits can be observed after vermal lesions in rats, it is not easy to relate them to the differential performance of the two groups on the three instrumental tasks. How, then, can the differences be accounted for? The hypothesis that vermal lesions change the reactivity of animals to reinforcers appears useful to the extent that it parsimoniously describes the differences between experimental and control groups. There is no assurance, however, that this hypothesis is valid. This restriction has to be imposed because the performance on tasks like the ones used in Experiment 2 is influenced by a variety of variables. One variable which is probably of importance is emotionality. It might be argued now, that some of the tests (open field, "time taken to leave cage") do measure emotionality to a certain extent. Unfortunately, these tests tend to confound emotionality and activity. That the factor of emotionality should be considered is suggested by the findings of Experiment 1.

Thus, in order to assess the role of any hypothetical

changes in reactivity to reinforcers more clearly, it would be desirable to find experimental conditions under which the factor of emotionality could be largely eliminated. The use of intracranial self-stimulation (ICSS) as reinforcer seemed to provide such conditions. Intracranial self-stimulation behavior can be developed in a non-stressful manner because animals become acquainted with the experimental setting over a long period of testing. In addition, the reinforcer is not aversive and its delivery is entirely under the control of the animal. Further advantages are that learning factors are minimized in ICSS which permits meaningful "before" and "after" comparisons in the same animal. Use of ICSS also makes it possible to match, operationally, experimental and control animals in their response to the reinforcer.

Experiment 3 was designed to test the effect of vermal lesions on ICSS behavior in rats.

Finally, and most importantly, the use of ICSS in the region of the lateral posterior hypothalamus provides an opportunity to investigate cerebellar influences on this area in terms of overt behavior. The potential importance of these influences has been discussed previously (pages 9 and 11) on the basis of physiological work. Cerebellar-hypothalamic interactions have also been suggested by electrophysiological (Ban et al., 1956; Whiteside & Snider, 1953) and anatomical (Larsell, 1967) investigations.

CHAPTER IV

EXPERIMENT 3

Any attempt to evaluate the effects of vermal lesions on ICSS must take into account the motor deficits resulting from such lesions. Conventionally, brain stimulation is contingent upon bar pressing. Rapid bar pressing requires motor skills, however, which are likely to be impaired after vermal lesions. For this reason, an instrumental response was selected which involved a minimum of motor skills; it consisted simply of touching a metal spout.

Method

Subjects- Twenty-eight male Montreal Black-Hooded rats, averaging 300 gm, were used. The animals were purchased from the Quebec Animal Laboratories. Subjects were housed singly.

Apparatus- Subjects were trained and tested in a 30 by 16 cm Lucite box with 30 cm walls. The Lucite box was contained in a large wooden box which was illuminated by a 10 W light. The grid floor of the Lucite box and

the metal spout of a graduated water bottle which was attached to the Lucite box were connected to a model 1925 Leheigh Valley Electronics Drinkometer. The metal spout protruded 2 cm into the interior of the Lucite box and was located 6 cm above the grid floor. If an animal touched the spout, a circuit was closed and the Drinkometer triggered a model 111-C Hunter Decade Interval Timer which in turn activated a 60 cycle sine wave variable current stimulator for 0.2 sec. Two model TCe24EY 6 V Sodeco Electronic counters were used to count the number of stimulations (triggered by the stimulator) and the total number of contacts (triggered by a second Drinkometer). A model 92 Rustrak Graphic Recorder, triggered by a model 100-C Hunter Decade Interval Timer could be switched into the circuit; the recorder was powered by a 24 V DC source. A four channel mercury commutator served to prevent twisting of the stimulating leads. The stimulating current could be monitored through a Telequipment two channel oscilloscope.

Procedure- Three to five days after having received electrode implants, subjects were placed on a 24 hr water deprivation schedule. The deprived animals were attached to the stimulating leads and placed into the Lucite box. They could obtain water by licking the metal spout of the graduated water bottle. By doing so, they received brain stimulation and ICSS behavior usually developed within two

or three testing sessions. Testing sessions lasted for 10 min and were given once daily. After ICSS behavior had been established, subjects were returned to ad libitum water consumption in their home cages and no more water was available in the testing situation.

Two categories of self-stimulators were defined: high rate (more than 1000 stimulations per 10 minutes) and low rate (less than 1000 stimulations per 10 minutes) self-stimulators. These categories were established at a current level of 30 μA for all animals. Since any possible upward changes in ICSS would be difficult to detect in the high rate animals, it was decided to lower their ICSS rates. This was accomplished by lowering the stimulus current in 5 μA steps to a final level of 10 μA for all high rate animals. For low rate animals the stimulus current was kept at 30 μA.

All animals were given testing sessions until no extreme upward or downward trends in ICSS were shown. When this point had been reached, usually after 14 days of testing, the animals were tested for an additional seven days. The average of the rates recorded on these seven days served as reference against which postoperative changes were to be compared. On Day 8, subjects received either sham-operations or ablations of the vermis. Two of the control subjects received small, unilateral ablations of the frontal cortex (Ss 38 and 96). Postoperative testing, under conditions identical to those employed on the

last seven testing days, resumed on Day 4 after surgery and extended for seven days.

Surgery- The stimulating electrodes were implanted at the transverse plane of the lateral posterior hypothalamus. Type MS 303-018"-312"-SS-010" twisted bipolar enamel-insulated electrodes (wire diameter 0.25 mm) from Plastic Products were used. All electrodes were cut straight and the tips were separated 0.5 mm to prevent current leaks. A coordinate system based on skull sutures was used for implantation. The skull was positioned in a stereotaxic holder so that bregma and lambda were on the same horizontal plane. The electrode was inserted 3.3 mm posterior to bregma and 1.7 mm lateral to the sutura sagittalis. For high rate subjects the electrodes were lowered 7.8 mm while for low rate subjects the electrodes were lowered about 7.0 mm. The electrodes were held in place by dental cement which was anchored on four stainless steel screws. All electrodes were tested for current leaks before insertion.

Vermal ablations were performed by aspiration. To gain access to the vermis, the medial part of the os interparietale and the os supraoccipitale were removed until both superior cerebellar veins were visible. The midline dorsal vermis from the caudal lobules of the declive to the pyramis was then aspirated. Both implantations and ablations were performed under sodium pentobarbitol (40 mg/kg, supplemented by 0.1 ml of 300 mg/ml

chloral hydrate, i.p.) anaesthesia. For sham-operations, two animals (Ss 38 and 96) received small, unilateral ablations of the left frontal cortex while in the remaining animals the vermis was exposed. An effort was made not to damage the dura mater.

Results

Tables 9 and 10 show that the ICSS rates of both high and low rate control groups did not change significantly after the sham-operations. Both control groups showed a non-significant decrease in rates after surgery. It can also be seen that the control and experimental groups did not differ significantly before surgery for both low and high rate self-stimulators. The rates of experimental low rate self-stimulators increased significantly after vermal lesions ($t = 3.70$, $p < 0.05$). The same held true for experimental high rate self-stimulators ($t = 2.61$, $p < 0.05$). Observation of the animals suggested that the motor deficits (which were similar to those described in Experiment 2) did not appreciably interfere with the performance of the instrumental response. The raw data underlying Tables 9 and 10 are presented in Tables 11, 12, 13 and 14.

While all animals were trained to self-stimulate by licking the spout, there was a tendency to self-stimulate by touching the spout with the paw or the snout

as soon as no more water was available in the testing situation. Inspection of the graphic records did not reveal any obvious qualitative changes in ICSS behavior after vermal lesions, nor did there seem to be any noticeable change in the ratio of total numbers of contacts to total number of stimulations.

Discussion

The increase in self-stimulation is consistent with the hypothesis that animals with vermal lesions differ from control animals in their reaction to reinforcers. However, alternative interpretations of changes in ICSS are available. Vermal lesions, for instance, might reduce the aversive components of brain stimulation. Aversive components are likely to have been present in low rate self-stimulators because these animals tended to show signs of discomfort if stimulation was administered by the experimenter at fast rates (4 stimuli per second). While the factor of aversive components might be of some importance in the ICSS increases in low rate subjects, there is no reason to believe that aversive components of brain stimulation are of significance with regard to high rate subjects.

Another possibility is pointed out by the findings of Routtenberg and Malsbury (1969). They showed that self-stimulation could be obtained in parts of the mid-

brain which are usually associated with extrapyramidal function. Vermal lesions might directly influence the activity levels in parts of the extrapyramidal system and therefore change the effectiveness of brain stimulation in sites involved with this system. It is interesting to note, in this context, that some of the electrode placements in this study were found to be located in Forel's fields H_1 and H_2 and in the zona incerta (Figure 8). These regions are traditionally associated with extrapyramidal function.

In view of the apparent functional division between the anterior and posterior cerebellum, it would have been of interest to find out what effects ablation of the anterior cerebellum would have on ICSS behavior. A pilot study suggested that the kind of motor deficits resulting from anterior cerebellar lesions in the rat (foreleg and, to a lesser extent, hindleg hypertonus, resulting in retropulsion and falling over backward) interfered severely with the instrumental response required to obtain ICSS. Thus, a direct comparison of anterior and posterior lesion effects is difficult.

Some thought should be given to the possibility that the changes in ICSS behavior are not related to any intrinsic properties of the brain stimulation. Observations made on cats and monkeys suggest that in these animals the responsiveness to extraneous auditory stim-

uli decreases after vermal lesions. Is it possible, then, that the increases in ICSS simply reflect the possibility that animals with lesions are less likely to be disturbed by extraneous noises (with resulting interruption of ICSS behavior)? To gain some insight into this question, a group of six rats with vermal lesions was compared to a group of six control animals in a situation which measured habituation to a sudden, loud noise. The animals were placed in an activity box which was connected to a graphic recorder and a 5 min activity record was taken. Subsequently, a sudden, loud noise was presented every 20 sec for 30 min in order to assess habituation to the sound. Habituation was defined as no detectable startle for five consecutive sound presentations. Table 15 indicates that the two groups did not differ significantly in the number of startle responses needed to reach habituation ($\underline{t} = 0.98$, $\underline{p} > 0.05$). Unfortunately, a direct comparison of the magnitude of the startle responses was not possible since the magnitude of a startle response depends strongly on whether the animal is moving or at rest, and the two groups differed significantly in their general activity (Table 16; $\underline{U} = 5$, $\underline{p} < 0.05$). It appeared that the animals with vermal lesions showed less gross movement than control animals. To measure the absence of gross movement, the sections of the graphic record which indicated lack of movement were converted from

length into time units. On the basis of these findings it may be concluded that the factor of attention to extraneous noises was probably not of crucial importance in bringing about the observed differences in ICSS between control and experimental groups.

Finally, it should be mentioned that the ICSS behavior of both low and high rate subjects became very erratic if the stimulation current was lowered towards threshold levels. For this reason, no attempts were made to investigate threshold differences before and after vermal lesions.

CHAPTER V

EXPERIMENT 4

Since removal of the dorsal midline vermis appears to bring about an increase in ICSS, it would be of interest to find out if self-stimulation rates can be manipulated by stimulation of this vermal region. Experiment 4 was carried out to investigate this possibility. In addition, the influence of anterior cerebellar stimulation on ICSS was also studied in order to see if stimulation of anterior and posterior vermal regions has similar or opposing effects on ICSS rates.

Method

Subjects- Eleven male Montreal Black-Hooded rats, averaging 300 gm, were used. The animals were purchased from the Quebec Animal Laboratories.

Apparatus- The apparatus was identical to the one used in Experiment 3. Cerebellar stimulation was delivered by a Tektronix Type 163 Pulse Generator, triggered by a Tektronix Type 162 Waveform Generator. The output of the stimulator was passed through a model

100 Bioelectric Stimulus Isolation Unit before reaching the animal. Two of the four channels of the mercury commutator were used to transmit the stimulus to the animal. Stimulation consisted of monophasic pulses of 1 msec duration at 100 Hz and about 1.5 V.

Procedure- Nine of the animals received electrode implants in the lateral posterior hypothalamic region. Five of the animals received a second electrode in the superficial anterior vermis (culmen and anterior border of sublobule a of the declive) while the other four animals received a second electrode in the posterior vermis (in the sublobules of folia VII and VIII). The remaining two subjects received an electrode in the right fastigial nucleus. The electrodes were of the type used in Experiment 3.

The subjects with hypothalamic electrodes were given one daily 10 min ICSS session until stable ICSS behavior appeared. All of these subjects self-stimulated at 30 μA. Subsequently, these animals were tested for 16 days with (VS) and without (NVS) vermal background stimulation according to the following schedule:
NVS VS VS NVS VS NVS NVS VS VS NVS VS NVS NVS VS VS NVS.
The testing sessions lasted for 10 minutes and on the VS days vermal background stimulation was given for the entire session while the animal self-stimulated at the hypothalamic site. After Day 16, the motor responses of

all animals to vermal stimulation of higher intensities were recorded. In addition, attempts were made to see if animals would self-stimulate at cerebellar sites.

Results

Table 17 shows that vermal background stimulation seemed to increase ICSS behavior in animals with electrodes in the anterior cerebellum ($t = 3.28$, $p < 0.05$) while vermal background stimulation did not seem to have a significant effect in animals with posterior cerebellar placements. The raw data underlying Table 17 is presented in Tables 18 and 19.

No overt motor behaviors were observed at the background stimulation intensities but if the voltages were increased to the 5-10 V range, there were obvious motor responses. It was not possible to clearly differentiate the effects of anterior and posterior cerebellar stimulation. Responses were, for the most part, bilateral. The most common responses consisted of a foreleg extension which was sometimes accompanied by a hindleg adduction. Extensor rebounds did not occur consistently but were observed. A response of the trunk musculature was noted frequently, particularly if the stimulation was maintained for more than 1 sec. At voltages near 9 V a flattening of the body was observed (the subjective impression was one of the animal's melting on the ground)

accompanied by extensor tonus and abduction of all four limbs. Occasionally, this response was accompanied by an adduction of the head to the chest. No obvious signs of discomfort were shown by the animals even at these high stimulus voltages.

A different response was obtained from animals with electrodes in the fastigial nucleus. Here, even low voltage (2-3 V) stimulation yielded a contralateral extensor tonus accompanied by ipsilateral extensor collapse. At voltages in excess of 3 V animals showed chewing responses and salivation as well as slight signs of discomfort. Squealing was observed at 5 V. Whether or not physical spread of current to the brain stem was responsible for the aversive responses is uncertain. After a lesion was produced at the stimulation site (2 mA for 20 sec), signs of discomfort could still be obtained at high voltages (10-15 V).

Discussion

Contrary to expectation, stimulation of the posterior vermis did not influence ICSS rates. It had been hoped that the stimulus frequency used (100 Hz) would have been optimal in producing effects since such high frequency stimulation is considered to have an excitatory effect (Dow & Moruzzi, 1958). The underlying assumption of the experiment was that stimulation of the vermis

would have effects opposite to those of ablation and that stimulation would result in a depression of ICSS behavior. Such a speculation was perhaps somewhat naive since the actual area of stimulation was in all likelihood much smaller than the area of ablation (the tips of the stimulating electrode were only 0,5 mm apart). In addition, the low voltage of stimulation may have been insufficient to produce appreciable results; higher voltages could not be applied due to the danger of confounding motor disturbances. The fact that anterior cerebellar stimulation did have effects on ICSS does not necessarily imply that this effect was based on mechanisms similar to those bringing about ICSS increases after vermal ablations. In fact, the effects of anterior cerebellar stimulation might be related to the general activation reaction seen after anterior cerebellar stimulation.

Self-stimulation at cerebellar sites was not observed. Attempts to elicit self-stimulation were made by conventional shaping procedures and also by presenting a cerebellar stimulus whenever the animals self-stimulated at a lateral hypothalamic site. Failure to obtain self-stimulation at cerebellar sites should not be taken to imply that self-stimulation in the cerebellum is not possible. Before such a negative statement can be made, a great number of stimulating parameters and experimental conditions will have to be explored.

CHAPTER VI

GENERAL DISCUSSION

A survey of the literature shows that the cerebellum influences autonomic functions and electrocortical activity. Incidental observations have suggested that these non-motor functions of the cerebellum may be important in terms of overt behavior but there has been no experimental investigation of this possibility. The purpose of this study was to find out whether cerebellar lesions result in non-motor behavioral changes in monkeys, cats, and rats. Three different dependent variables were used to demonstrate these changes.

The first variable involved changes in affective behavior after cerebellectomies and vermal lesions in cats and vermal lesions in monkeys. The changes in cats were in agreement with observations made by Chambers and Sprague (1955) and Sprague and Chambers (1959). The changes in both cats and monkeys were in the direction of greater tractability. All effective lesions (effective in terms of producing greater tractability) damaged the tuber and folium vermis. The second variable was the performance of rats with

vermal lesions on instrumental tasks concerned with the response to food and electrical shock. It was found that the animals with vermal lesions differed from the control animals. The difference was tentatively attributed to a changed reactivity of animals with vermal lesions to reinforcers. The third variable was the rate of ICSS in rats before and after vermal ablations and during cerebellar stimulation. Vermal ablations and stimulation of the anterior vermis tended to raise ICSS rates while posterior vermis stimulation appeared to have no effect on ICSS. The changes in these three variables after cerebellar manipulation support the contention that the cerebellum is involved in non-motor function.

Any attempt to postulate a single mechanism underlying these various findings appears premature but it may be of interest to examine a number of possibilities.

Glickman and Schiff (1967) proposed that the activation of neural elements underlying the elaboration of species specific motor patterns may, in itself, constitute a sufficient condition for reinforcement. They further suggested that the activation of circuits underlying approach behavior is positively reinforcing while activation of circuits underlying withdrawal behavior is negatively reinforcing. Part of Glickman and Schiff's theory is that the circuitry underlying species specific motor patterns is located in the reticular formation of the brain stem (see also Zanchetti, 1967) The cerebellum

exerts influences on elements of the reticular system and it may be suggested that a chronically altered cerebellar influence on the circuitry subserving species specific motor patterns may alter the response of an organism to reinforcers. While this explanation might account for the increased rates in self-stimulation and the differential responses to food and shock in rats after vermal lesions, it cannot easily explain the changes in cats and monkeys. Such changes were observed in one direction only and it is not immediately obvious why approach and withdrawal behaviors should not be equally affected. This last point assumes that there is an equal representation of approach and withdrawal behaviors. Self-stimulation studies indicate, however, that far fewer points in the brain yield aversive effects than positive effects. Thus, more neural elements may be involved with approach behaviors than with withdrawal behaviors. ("Affective" changes in the direction of friendliness only have been observed by MacLean in 1957 during hippocampal seizures in cats). Also, there is no immediate reason why withdrawal (aversive) components should be prevalent in simple handling of animals. The behavioral changes in cats, rats, and monkeys after vermal lesions could therefore be interpreted within the framework of Glickman and Schiff's (1967) biological theory of reinforcement.

Other explanations, however, are available. The cerebellar influences on the autonomic system could be involved

in the following way. Singer (1961) showed that rats injected with epinephrine did not differ from control animals in a familiar setting. In a fear-provoking setting, however, epinephrine injected rats reacted significantly differently from control animals. What Singer had done was to change the background level of autonomic activity which resulted in changed overt responses to a stressful condition. Similarly, the cerebellar lesions in this study could have an influence on the background levels in the autonomic system which, in turn, brought about behavioral changes under the training conditions used with the rats. It is at this point not possible to provide a meaningful argument about the direction of the presumed autonomic changes since physiological data do not warrant such a step. Changes in behavioral responses due to changes in autonomic reactivity or changes in autonomic background activity may account for the responses of rats to shock or for changes in self-stimulation but do not readily provide an explanation for the changes observed in cats and monkeys.

A more inclusive explanation of non-motor behavioral changes after vermal lesions, but less useful in terms of testable predictions, might stress the evidence which suggests that the extrapyramidal system is more intimately related to affective processes than is commonly thought. Circumstantial evidence related to this point is not difficult to find. Hypnotists, for instance, find

it quite difficult to suggest a mood (e.g. joy) which stands in contradiction to a previously suggested posture (lowered head, drooping shoulders) in a hypnotized subject (Pasquarelli & Bull, 1951). Conversely, if a mood is suggested, the hypnotized subject usually assumes a posture appropriate to the mood (Gidro-Frank, 1950). Freyhan (1957) indicated that reversible symptoms of Parkinsonism developed in patients treated with chlorpromazine and reserpine. These drugs are generally prescribed for mental patients suffering from increased affective tension and hypermotility. Further evidence for the possibility of direct extrapyramidal - affective interactions are indicated by a variety of clinical observations. Patients with Wilson's disease (which affects some parts of the basal ganglia) are often prone to spontaneous fits of laughter and crying and the mask-like facial expression of patients suffering from paralysis agitans is well known. A dissociation between emotionally induced and voluntary facial movements can often be observed contralaterally to an occluded superior cerebellar artery. More direct evidence, however, is available. Sem-Jacobsen (1968) presented the results of stimulation of extrapyramidal structures in humans and changes in mood, autonomic changes, and changes in alertness were observed. Changes in mood were obtained very frequently in sites which, at higher voltages, yielded

motor responses of the head and face. The possible special significance of facial movement in the elaboration of affective processes has been considered by Gellhorn (1967) who speculated that "facial cutaneous and proprioceptive impulses play an important role in facilitating the complex interactions between brainstem and limbic and neocortex which occur during emotion and contribute to the variety of cortical patterns of excitation which underlie specific emotions" (p. 165). It should be noted in this context that the cerebellar regions ablated in Experiments 1, 2, and 3 of this paper are regions which receive tactile input from the face (Brodal, 1967).

Routtenberg and Malsbury (1969), on the basis of self-stimulation studies in rats, have directly related extrapyramidal structures to processes of reinforcement.

In view of the preceding considerations, the non-motor behavioral changes after cerebellar manipulation may merely be another manifestation of extrapyramidal involvement in non-motor function.

The search for factors which may be involved in non-motor behavioral changes after cerebellar manipulation is not exhausted. Newman and Feldman (1964) reported that rewarding intracranial stimulation is accompanied by afterdischarges. It may be recalled at this point that

Iwata and Snider (1959) demonstrated cerebellar influences on hippocampal seizure activity; such seizure activity has been related to affective changes by MacLean (1957). While the following suggestion is highly speculative, it is certainly intriguing. Could it be that afterdischarges are related to processes of reinforcement? Further, could it be that the cerebellum plays an important role in the regulation of such afterdischarges? If this were the case, then the cerebellum might be involved in this particular non-motor function by regulating the mechanisms the action of which is reflected in the afterdischarges.

At this point the question might arise: why has there been no attempt to relate recent electrophysiological work (Eccles, Ito, & Szentagothai, 1967) to the behavioral findings under discussion? Let it be assumed, for the moment, that the behavioral changes can be interpreted with help of what is known about cerebellar electrophysiology. Such an argument would be based on the idea that the cerebellar nuclei have an excitatory influence on their target neurons and are under inhibitory control by the Purkinje cells of the cerebellar cortex. Removal of the cerebellar cortex would remove such inhibition and result, presumably, in a release of cerebellar nuclear activity. The increased nuclear outflow, then, might be responsible for whatever changes occur. There is, however, no guarantee that Purkinje cell activity must always inhibit nuclear cells.

Deura (1969) found that cortical cerebellar stimulation resulted in nuclear excitation. He speculated that interneurons were involved and indicated that a variety of cortico-nuclear interactions were possible. Thus, the nature of nuclear outflow to particular target cells after cerebellar cortical ablations is not easily predicted. But even if the nature of this outflow were known, one would still have to know whether the target cells themselves belong to inhibitory or excitatory systems. The divergent effects of lesions in different regions of the fastigial nuclei suggest that even though the fastigial outflow may be excitatory, the behavioral consequences depend entirely on the location of the fastigial lesion and therefore on the nature of the target cells. Thus, the effects of a certain cerebellar lesion, and in particular the generally unexplored posterior vermis, on activity at the second synapse cannot be predicted on the basis of existing electrophysiological data. It is felt, therefore, that attempts to relate the observed behavioral changes to electrophysiological research will require too many assumptions to be of value at this point.

The poverty of auditory and visual attention, as observed in monkeys and cats implicates the cerebellum in yet another aspect of non-motor function. Of particular interest is the fact that animals reacted differentially to meaningful and extraneous noises and that the deficits

are not likely due to threshold changes. It is possible that the auditory and visual functions of the cerebellum are related to collicular activity. The colliculi have extensive connections to the brain stem reticular formation and might be concerned with a feedback mechanism which maintains appropriate levels of activity in the visual cortex. The collicular connections with the cerebellum might serve to communicate to the cerebellum nonspecific general levels of activity in the visual system which the cerebellum utilizes in order to modulate general levels of activity in all sensory systems through nonspecific ascending pathways.

While both monkeys and cats with damage to the folium and tuber vermis showed an obvious deficiency in auditory startle, such a deficiency could not be seen in rats. It will be recalled that no significant differences were noted between rats with vermal lesions and control animals in the number of startle responses required to habituate to a loud noise. Nevertheless, technical difficulties did not permit conclusive evaluation of the magnitude of the startle responses (the background motor activity confounded the magnitude of the startle), and it is entirely possible that the startle reaction of animals with vermal lesions was less marked. In addition, the intensity of the noise was quite high and further work with lower intensities may yield differences in startle. A certain subtle poverty of movement was noted in all animals with

vermal lesions and may constitute a characteristic motor deficit after damage of the posterior vermis.

In the discussion of motor deficits after vermal lesions in cats, monkeys, and rats, it was suggested that formalized testing procedures might be useful in evaluating such deficits. Jumping deficits in all of these species, for instance, could be investigated with help of jumping stands of the kind used in visual discrimination experiments (Mahut, 1954). The distance between start and landing points could be varied and the force of jumps could be measured by connecting the platform to a weighing scale with a graphic recorder. With cats and monkeys the accuracy and speed of reaching could be tested by using a rotating disk from which a morsel of food would have to be snatched. In addition, a variety of tasks requiring fast locomotion or a sense of balance (the monkeys with vermal lesions were never seen to walk on a rope which stretched through their enclosure after surgery) might be used. For rats, a motor driven variable speed running wheel might prove useful. Use of such testing procedures would improve the chances of identifying and defining motor deficits after small cerebellar lesions. In addition, the findings could be communicated efficiently and without ambiguity.

Summary

A review of the literature indicates that the cerebellum participates in the regulation of autonomic functions and electrocortical activity. On the basis of this evidence as well as incidental observations of affective changes after cerebellar manipulation in the literature, it was hypothesized that cerebellar lesions or stimulation should result in overt non-motor behavioral changes. The objective of this thesis was to demonstrate such changes.

Non-motor behavioral changes after ablations of the posterior cerebellar vermis in monkeys, cats, and rats were described. Monkeys and cats became more docile and tractable and appeared less alert after surgery. Enhanced pleasure reactions were observed in cats with posterior cerebellar ablations. Rats with posterior vermal lesions took less time, initially, to approach the food in a food-approach task than did sham-operated rats. Rats with posterior vermal lesions performed better than sham-operated animals on a passive shock avoidance task and on the second reversal of an active avoidance task. In addition, posterior vermal lesions in rats were shown to increase intracranial self stimulation in the lateral posterior hypothalamic region. Background stimulation of the anterior cerebellar vermis increased intracranial self stimulation at lateral posterior hypothalamic sites while background stimulation of the posterior cerebellar vermis was found to be without effect.

These results demonstrate that lesions or stimulation of the cerebellum can result in overt non-motor behavioral changes. A number of hypotheses were advanced in order to account for these changes. The most interesting hypothesis, underlined by known ascending anatomical projections of the cerebellum, is that the cerebellum can directly modulate activity in the neural substrate underlying processes of reinforcement.

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APPENDIX

Table 1

Time taken to reach food

Ss	Day 1	2	3	4	5	$\bar{X}$	6	7	8	9	10	$\bar{X}$	
1	18.4*	6.0	3.1	6.0	4.3	7.6	11.8	12.9	5.4	3.2	2.9	7.2	Vermis Lesions
2	9.9	2.0	2.1	1.7	1.6	3.5	1.7	1.8	1.6	1.6	1.6	1.7	
3	15.3	13.1	8.8	6.4	7.3	10.2	7.6	4.4	2.8	2.1	2.4	3.9	
4	17.2	4.0	3.5	3.0	4.0	6.3	4.5	3.4	2.3	2.0	1.9	2.8	
5	16.2	7.1	2.6	5.2	3.0	6.8	6.2	2.4	1.6	1.5	1.9	2.7	
6	7.6	4.5	2.8	2.7	1.8	3.9	2.0	2.1	3.1	2.2	1.6	2.2	
7	12.1	5.5	5.5	4.4	4.6	6.4	7.6	6.1	4.0	3.0	2.9	4.7	
8	11.6	12.8	12.1	9.7	7.7	10.8	4.0	2.6	2.5	3.2	1.6	2.8	
9	17.6	8.3	11.5	8.4	6.9	10.5	9.1	4.1	3.3	3.0	2.6	4.4	
10	21.1	29.0	4.7	5.9	4.5	13.0	4.9	4.7	4.3	3.8	3.5	4.2	
$\bar{X}$	14.7	9.2	5.7	5.3	4.6	7.9	5.9	4.5	3.1	2.6	2.3	3.7	
11	120.	98.8	62.9	120.	53.1	90.9	2.3	2.0	1.6	1.1	1.5	1.7	Sham-Operations
12	9.7	3.0	4.0	2.0	2.1	4.2	1.5	1.5	1.2	1.3	1.2	1.3	
13	32.6	14.4	5.4	3.3	1.7	11.3	1.4	1.2	1.1	1.1	1.1	1.2	
14	26.5	22.2	4.9	3.9	2.5	12.0	2.1	1.6	1.5	1.1	1.1	1.5	
15	24.2	13.0	31.6	23.3	1.8	18.8	1.5	1.4	2.8	1.4	1.1	1.6	
16	31.7	9.5	2.6	2.7	2.1	9.7	1.7	1.6	1.5	1.6	1.4	1.6	
17	120.	120.	120.	38.3	13.1	82.3	1.1	2.5	2.3	1.6	1.1	1.7	
18	9.7	2.0	2.1	1.6	1.7	3.4	3.5	1.1	1.1	1.1	1.1	1.6	
19	52.7	80.0	16.5	5.2	4.3	31.7	1.8	1.7	1.4	1.2	1.3	1.5	
20	120.	120.	120.	6.9	10.1	75.4	20.3	3.1	2.4	1.9	1.5	5.8	
$\bar{X}$	54.7	48.2	37.0	20.6	9.3	34.0	3.7	1.8	1.7	1.3	1.2	2.0	

*Scores represent the median of five latencies, measured in seconds

Table 2

Avoidance latencies during the first eight days of training in the shuttle box

Vermis Lesions

Ss	Day 1	2	3	4	5	6	7	8	$\bar{X}$
1	3.8*	1.8	2.0	2.4	2.8	2.0	2.6	3.0	2.6
2	6.4	1.4	1.2	1.6	1.4	1.2	1.4	1.8	2.1
3	5.4	5.4	4.8	4.4	5.0	3.0	3.6	4.6	4.5
4	3.8	2.4	3.4	2.4	2.6	3.6	1.8	1.8	2.7
5	6.2	6.2	2.8	1.8	1.6	1.4	1.2	1.4	2.8
6	5.4	4.0	1.4	1.4	5.6	2.0	2.0	1.6	2.9
7	3.0	1.2	1.2	5.0	2.2	1.6	1.8	2.0	2.3
8	3.4	5.4	3.0	1.2	3.2	3.2	2.4	3.8	3.2
9	7.0	6.2	6.2	6.0	3.0	3.8	3.0	4.0	4.9
$\bar{X}$	4.9	3.8	2.9	2.9	3.0	2.4	2.2	2.7	$\bar{\bar{X}}$ 3.1

Sham-Operations

Ss	Day 1	2	3	4	5	6	7	8	$\bar{X}$
11	5.8	2.8	2.0	5.6	2.2	1.8	4.2	1.8	3.3
12	2.0	2.0	2.6	1.6	4.0	1.3	1.8	1.6	2.0
13	3.6	1.8	1.4	1.4	1.4	1.4	1.6	2.8	1.9
14	5.4	1.6	1.4	4.2	1.4	1.4	1.2	1.4	2.3
15	4.8	1.6	4.8	2.2	1.4	1.6	1.8	2.0	2.5
16	5.4	3.0	2.8	1.8	3.0	2.2	4.2	2.0	3.1
17	6.4	6.0	1.6	1.6	1.2	1.8	1.4	2.2	2.8
18	6.0	3.6	2.0	1.8	1.8	1.6	1.4	1.2	2.4
19	5.4	1.8	1.4	1.4	1.2	1.4	1.2	1.8	2.0
$\bar{X}$	5.0	2.7	2.2	2.4	1.7	1.8	2.1	1.9	$\bar{\bar{X}}$ 2.5

Comparison of means of medians, collapsed over days:
$t = 0.54$, $p > 0.05$; t test for independent samples

* Scores represent median of three latencies, in seconds

Table 3

Avoidance latencies during the second eight days of training in the shuttle box

Vermis Lesions

Ss	Day 1	2	3	4	5	6	7	8	$\bar{X}$
1	8.2*	6.4	1.4	1.4	1.6	1.4	1.4	1.6	2.9
2	9.4	5.8	2.4	5.6	4.4	1.8	1.6	1.4	4.1
3	6.0	7.2	5.6	2.0	3.8	2.2	2.2	1.6	3.8
4	9.0	6.0	3.4	3.0	1.6	2.4	1.6	1.8	3.6
5	11.8	5.6	3.4	1.4	1.2	3.0	1.4	1.8	3.7
6	6.4	5.8	5.4	1.8	1.2	1.6	1.6	1.6	3.2
7	6.0	6.0	1.6	1.2	1.0	1.0	1.4	1.0	2.4
8	17.4	5.0	2.8	2.0	2.0	4.0	3.0	3.2	4.9
9	15.2	5.4	4.0	2.8	2.0	2.6	2.6	2.8	4.7
$\bar{X}$	9.9	7.6	3.3	2.4	2.1	2.2	1.9	1.9	$\bar{\bar{X}}$ 3.7

Sham-Operations

Ss	Day 1	2	3	4	5	6	7	8	$\bar{X}$
11	7.4	6.0	5.8	6.0	3.8	4.6	2.4	3.6	6.0
12	7.0	7.8	5.6	4.4	2.8	2.6	2.2	2.0	4.3
13	12.0	6.4	4.8	1.2	1.4	1.8	1.4	1.2	3.8
14	6.2	7.0	4.6	1.6	1.4	1.2	1.6	3.2	3.4
15	7.8	4.8	1.0	1.2	2.0	1.0	2.0	1.4	2.7
16	6.0	7.0	2.0	5.8	1.6	0.8	2.2	1.4	3.4
17	6.2	6.2	3.0	5.8	2.9	1.6	1.8	1.2	3.5
18	7.0	5.4	6.0	1.8	1.4	1.4	4.0	1.2	3.2
19	11.6	5.6	5.6	2.4	1.4	1.8	1.8	5.2	4.4
$\bar{X}$	7.9	6.2	4.3	3.4	2.0	1.9	2.2	2.3	$\bar{\bar{X}}$ 3.9

Comparison of means of medians, collapsed over days: $t = 0.31$, $p > 0.05$; t test for independent samples

*Scores represent median of three latencies, in seconds

Table 4

Avoidance latencies during the third eight days of training in the shuttle box

Vermis Lesions

Ss	Days 1	2	3	4	5	6	7	8	$\bar{X}$
1	5.6*	2.6	2.0	1.4	1.8	2.4	2.2	2.4	2.6
2	6.4	5.4	2.4	1.2	1.4	1.4	1.4	1.8	2.7
3	6.2	5.8	2.8	1.8	1.4	2.2	1.8	2.8	3.1
4	6.0	2.4	1.8	1.6	1.4	1.0	1.2	1.6	2.1
5	7.2	1.4	4.0	1.4	1.4	1.8	1.8	1.6	2.6
6	1.2	1.4	1.4	1.4	1.6	1.6	1.4	1.4	1.4
7	5.8	1.2	1.0	1.0	1.0	1.0	1.2	1.2	1.7
8	2.0	1.8	1.4	1.4	2.0	2.0	1.8	1.8	1.8
9	1.6	2.2	1.6	2.2	2.4	2.4	2.6	2.6	2.2
$\bar{X}$	4.7	2.7	2.0	1.5	1.6	1.8	1.7	1.9	$\bar{\bar{X}}$ 2.2

Sham-Operations

Ss	Days 1	2	3	4	5	6	7	8	$\bar{X}$
11	5.8	5.8	5.8	1.8	3.6	2.6	3.2	2.4	3.9
12	6.0	5.8	5.4	2.8	1.4	5.4	4.2	2.8	4.2
13	8.0	5.8	1.4	1.4	1.2	1.4	1.4	1.4	2.8
14	5.6	5.6	5.4	2.6	2.4	4.2	1.4	1.2	3.6
15	6.4	2.4	3.0	2.2	0.8	1.2	1.4	0.6	2.3
16	6.0	5.4	3.2	2.2	1.6	1.2	1.4	1.2	2.8
17	5.6	2.4	2.6	1.4	1.8	2.6	3.0	2.6	2.8
18	5.6	6.0	3.4	1.4	1.4	1.2	1.0	1.0	2.6
19	5.4	2.0	1.8	2.8	5.0	2.4	1.4	3.2	3.0
$\bar{X}$	6.0	4.6	3.6	2.1	2.1	2.5	2.0	1.8	$\bar{\bar{X}}$ 3.1

Comparison of means of medians, collapsed over days: $t = 2.78$, $p < 0.05$; t test for independent samples

*Scores represent median of three latencies, in seconds

Table 5

Open Field Performance

Vermis Lesions		Sham-Operations	
Subjects	Crossings*	Subjects	Crossings
1	43	11	87
2	99	12	43
3	85	13	120
4	52	14	115
5	124	15	82
6	107	16	115
7	48	17	89
8	60	18	87
9	98	19	109
10	96	20	113
$\bar{X}$	81.2	$\bar{X}$	96.0

The difference between the group means was not significant ($t = 1.89$, $p > 0.05$; t test for independent samples)

*Number of fields crossed within 10 minutes

Table 6

Open Field Performance

Vermis Lesions		Sham-Operations	
Subjects	Crossings*	Subjects	Crossings
211	15	221	7
212	24	222	4
213	14	223	44
214	32	224	0
215	45	225	43
216	25	226	56
217	21	227	24
218	4	228	6
219	21	229	70
$\bar{X}$	22.3	$\bar{X}$	28.2

The difference between the group means was not significant ($t = 1.73$, $p > 0.05$; t test for independent samples)

*Number of fields crossed within 5 minutes

Table 7

Activity Wheel Performance

Vermis Lesions		Sham-Operations	
Subjects	Revolutions*	Subjects	Revolutions
1	37	11	604
2	38	12	465
3	446	13	47
4	373	14	209
5	171	15	153
6	944	16	86
7	27	17	251
8	238	18	200
9	144	19	194
10	222	20	260
$\bar{X}$	264	$\bar{X}$	246

The difference between group means was not significant ($t = 0.049$, $p > 0.05$; t test for independent samples)

*Number of activity wheel revolutions within 10 hours

Table 8

Time taken to leave cage

Vermis Lesions		Sham-Operations	
Subjects	Seconds*	Subjects	Seconds
1	315	11	406
2	780	12	241
3	434	13	36
4	180	14	273
5	195	15	1800
6	118	16	290
7	460	17	805
8	975	18	299
9	431	19	1800
10	931	20	1800
$\bar{X}$	481	$\bar{X}$	775

The difference between the groups was not significant ($\underline{U} = 47$, $p > 0.05$; Mann-Whitney $\underline{U}$ test)

*Seconds taken to leave the cage

Table 9

Comparison of average self-stimulation responses before and after surgery for low rate self-stimulators

	Control			Experimental	
Ss	PRSS*	POSS*	Ss	PRSS	POSS
27	177.3	117.4	61	567.4	652.1
67	330.1	253.4	65	720.3	928.7
75	128.7	112.3	71	204.8	271.1
76	204.1	145.4	74	59.4	96.4
95	460.1	507.4	80	164.1	216.3
96	455.4	451.8	84	19.6	29.6
111	356.0	279.5	90	592.3	756.3
			94	507.2	581.0
$\bar{X}$	301.7	266.7			
			$\bar{X}$	354.4	441.4

PRSS = Average of self-stimulation responses over seven preoperative test days.

POSS = Average of self-stimulation responses over seven postoperative test days.

Significance of differences between means:

PRSS Control - PRSS Experimental: $t = 0.47$, $p > 0.05$; t test for independent samples.

PRSS Control - POSS Control: $t = 2.22$, $p > 0.05$; t test for correlated samples.

PRSS Experimental - POSS Experimental: $t = 3.70$, $p < 0.05$; t test for correlated samples.

Table 10

Comparison of average self-stimulation responses before and after surgery for high rate self-stimulators

Control			Experimental		
Ss	PRSS*	POSS*	Ss	PRSS	POSS
21	46.7	15.3	23	20.7	461.0
31	156.7	50.6	28	169.9	153.8
33	73.4	35.6	32	95.1	208.3
34	33.4	51.7	39	94.4	159.4
38	236.4	193.6	41	29.9	85.0
41	45.6	29.9	62	90.3	151.9
			63	121.1	324.4
$\bar{X}$	98.7	62.8	69	174.1	168.0
			$\bar{X}$	100.9	214.9

PRSS = Average of self-stimulation responses over seven preoperative test days.

POSS = Average of self-stimulation responses over seven postoperative test days.

Significance of differences between means:

PRSS Control - PRSS Experimental: $t = 0.06$, $p > 0.05$; t test for independent samples.

PRSS Control - POSS Control: $t = 2.20$, $p > 0.05$; t test for correlated samples.

PRSS Experimental - POSS Experimental: $t = 2.61$, $p < 0.05$; t test for correlated samples.

Table 11

ICSS rates before and after sham-operations for low rate self-stimulators (control group)

	Ss	27	67	75	76	95	96	111
Preoperative Day	1	142	110	155	226	418	415	452
	2	54	198	71	172	411	440	411
	3	304	412	100	271	435	427	330
	4	282	340	144	71	528	438	292
	5	240	440	119	356	466	417	301
	6	56	478	146	188	499	571	355
	7	163	333	166	145	464	480	351
	$\bar{X}$	177.3	330.1	128.7	204.1	460.1	455.4	356.0
Postoperative Day	1 *	362	330	153	252	494	536	321
	2	2	202	115	179	508	404	300
	3	299	261	121	64	548	459	433
	4	34	317	134	108	507	483	227
	5	9	290	94	114	430	416	252
	6	107	139	74	136	510	467	230
	7	9	235	94	165	555	398	194
	$\bar{X}$	117.4	253.4	112.3	145.5	507.4	451.8	279.5

* Postoperative test Day 1 represents the fourth day after surgery

Table 12

ICSS rates before and after vermal ablations for low rate self-stimulators (experimental group)

	Ss	61	65	71	74	80	84	90	94
Preoperative Day	1	459	899	154	40	169	23	599	518
	2	592	597	157	92	139	6	619	411
	3	566	769	259	96	196	28	599	543
	4	614	883	149	86	162	19	587	496
	5	564	729	256	47	152	11	504	458
	6	640	610	218	31	165	28	607	542
	7	537	555	241	24	166	22	631	584
	$\bar{X}$	567.4	720.3	204.8	59.4	164.1	19.6	592.3	507.4
Postoperative Day	1	543	935	253	128	204	14	749	573
	2	666	942	292	74	220	19	757	628
	3	653	945	255	58	254	8	716	565
	4	688	953	285	96	350	26	752	554
	5	688	915	261	147	256	45	721	570
	6	672	933	255	74	112	58	810	580
	7	655	978	279	98	118	37	789	597
	$\bar{X}$	652.1	928.7	271.1	96.4	216.3	29.6	756.3	581.0

Table 13

ICSS rates before and after sham-operations for high rate self-stimulators (control group)

	Ss	21	31	33	34	38	41
Preoperative Day	1	70	200	100	45	887	64
	2	65	207	87	47	127	60
	3	43	204	64	22	65	4
	4	26	123	125	54	185	72
	5	16	154	44	25	174	32
	6	44	62	64	14	62	26
	7	63	147	30	26	110	61
	$\bar{X}$	46.7	156.7	73.4	33.3	236.4	45.6
Postoperative Day	1	0	77	20	65	163	72
	2	0	84	96	27	124	15
	3	23	61	14	53	108	22
	4	40	34	38	105	324	31
	5	20	13	25	37	249	9
	6	9	48	20	51	116	37
	7	15	37	11	24	271	23
	$\bar{X}$	15.3	50.6	35.6	51.7	193.6	29.9

Table 14

ICSS rates before and after vermal ablations for high rate self-stimulators (experimental group)

	Ss	23	28	32	39	41*	62	63	69
Preoperative Day	1	40	47	100	79	72	6	130	155
	2	10	572	82	56	15	174	95	98
	3	9	58	97	219	22	277	142	94
	4	28	37	60	108	31	20	51	189
	5	6	205	120	96	9	63	57	163
	6	38	218	118	96	37	40	173	303
	7	14	52	89	7	23	52	200	217
	$\bar{X}$	20.7	169.9	95.1	94.4	29.9	90.3	121.1	174.1
Postoperative Day	1	311	209	50	210	165	81	315	133
	2	444	196	137	218	45	132	172	286
	3	440	294	193	147	46	161	338	164
	4	553	119	219	59	75	190	348	114
	5	500	107	218	88	51	240	495	279
	6	521	75	251	225	85	91	317	101
	7	458	104	390	169	53	168	286	99
	$\bar{X}$	461.0	153.8	208.3	159.4	85.0	151.9	324.4	168.0

*Animal 41 was used as control and as experimental subject. At first, it received a sham-operation and seven days after the first day of postoperative testing it received a vermal ablation.

Table 15

Number of startle responses shown before habituation to sudden presentation to a loud sound

Vermis Lesions		Sham-Operations	
Subjects	Startle*	Subjects	Startle
151	56	161	52
152	26	162	22
153	55	163	26
154	29	164	62
155	12	165	64
156	60	166	90
$\bar{X}$	38.8	$\bar{X}$	52.5

The difference between the group means was not significant ($t = 0.98$, $p > 0.05$; t test for independent samples)

*Number of startle responses

Table 16

Time spent without gross movement in an activity box

Vermis Lesions		Sham-Operations	
Subjects	Seconds*	Subjects	Seconds
151	340	161	325
152	746	162	307
153	584	163	371
154	191	164	170
155	583	165	125
156	370	166	30
$\bar{X}$	469.0	$\bar{X}$	221.3

The two groups differed significantly ($U = 5$, $p < 0.05$; Mann-Whitney U test)

*Number of seconds spent without gross activity out of a total of 1800 seconds

Table 17

Average number of self-stimulations on the eight VS and NVS days for animals with anterior and posterior vermal implants

Anterior Vermis Implants

Subjects	VS	NVS
301	1123*	1085*
302	844	600
303	466	403
304	1085	984
305	1389	1224
$\bar{X}$	981.4	859.2

$t = 3.28$, $p < 0.05$; t test for correlated samples

Posterior Vermis Implants

Subjects	VS	NVS
306	1227	1227
307	168	212
308	955	999
309	613	612
$\bar{X}$	740.8	762.5

$t = 1.94$, $p > 0.05$; t test for correlated samples

*Number of self-stimulations

Table 18

Number of self-stimulations by rats with and without background stimulation in the anterior vermis

Vermis background stimulation

Session	2	3	5	8	9	11	14	15	$\bar{X}$
Ss									
301	1165	1104	1382	1008	1067	1285	895	1078	1123
302	910	925	604	898	918	941	658	898	844
303	599	359	343	317	513	546	378	678	466
304	1030	1005	850	1088	1141	1440	1086	1046	1085
305	1384	1380	1400	1400	1382	1273	1484	1412	1389

No vermis background stimulation

Session	1	4	6	7	10	12	13	16	$\bar{X}$
Ss									
301	1053	975	1159	1067	930	1240	1064	1194	1085
302	409	828	393	712	852	738	485	390	600
303	444	742	291	30	332	597	449	362	403
304	977	1062	768	951	1029	938	1085	1064	984
305	1313	1165	1212	1425	1175	1290	956	1259	1224

Table 19

Number of self-stimulations by rats with and without background stimulation in the posterior vermis

Vermis background stimulation

Session	2	3	5	8	9	11	14	15	$\bar{X}$
Ss									
306	578	578	613	624	640	630	660	584	612
307	1009	1174	1236	1222	1408	1261	1234	1278	1227
308	190	92	255	233	153	160	90	--*	168
309	878	872	862	989	1030	1125	818	1073	956

No vermis background stimulation

Session	1	4	6	7	10	12	13	16	$\bar{X}$
Ss									
306	581	561	673	619	671	652	597	555	613
307	1059	1161	1281	1108	1352	1232	1302	1322	1227
308	183	299	225	234	209	171	160	--	212
309	1024	935	901	1010	913	1000	1081	1135	1000

*Animal 308 died after Day 14

Figure 1

Example of a posterior vermal lesion in a monkey (monkey 1).

Figure 2

Example of a posterior vermal lesion in a cat (cat 4).

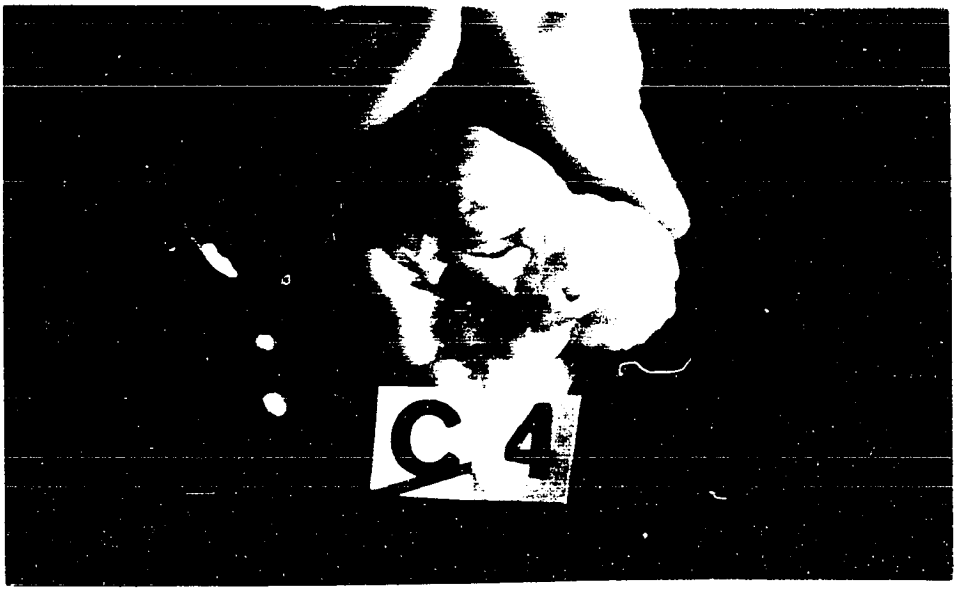

C4

Figure 3

Example of a cerebellectomy in a kitten (kitten 27).

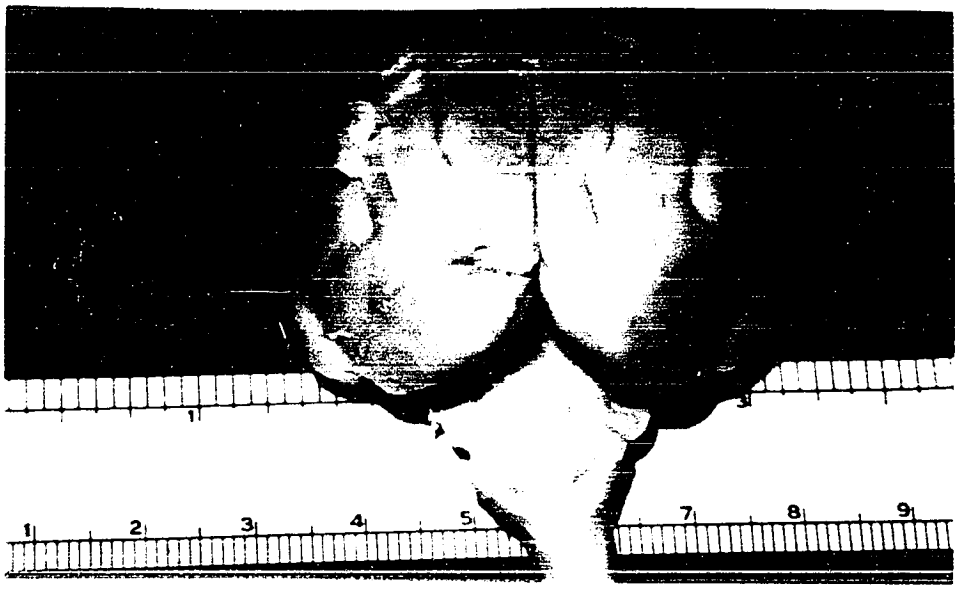

1
1
2
3
4
5
7
8
9

Figure 4

Performance of animals with vermal lesions and sham-operated animals on the Food Approach task. The performance scores are based on the mean of the median latencies achieved by each group on the daily trials.

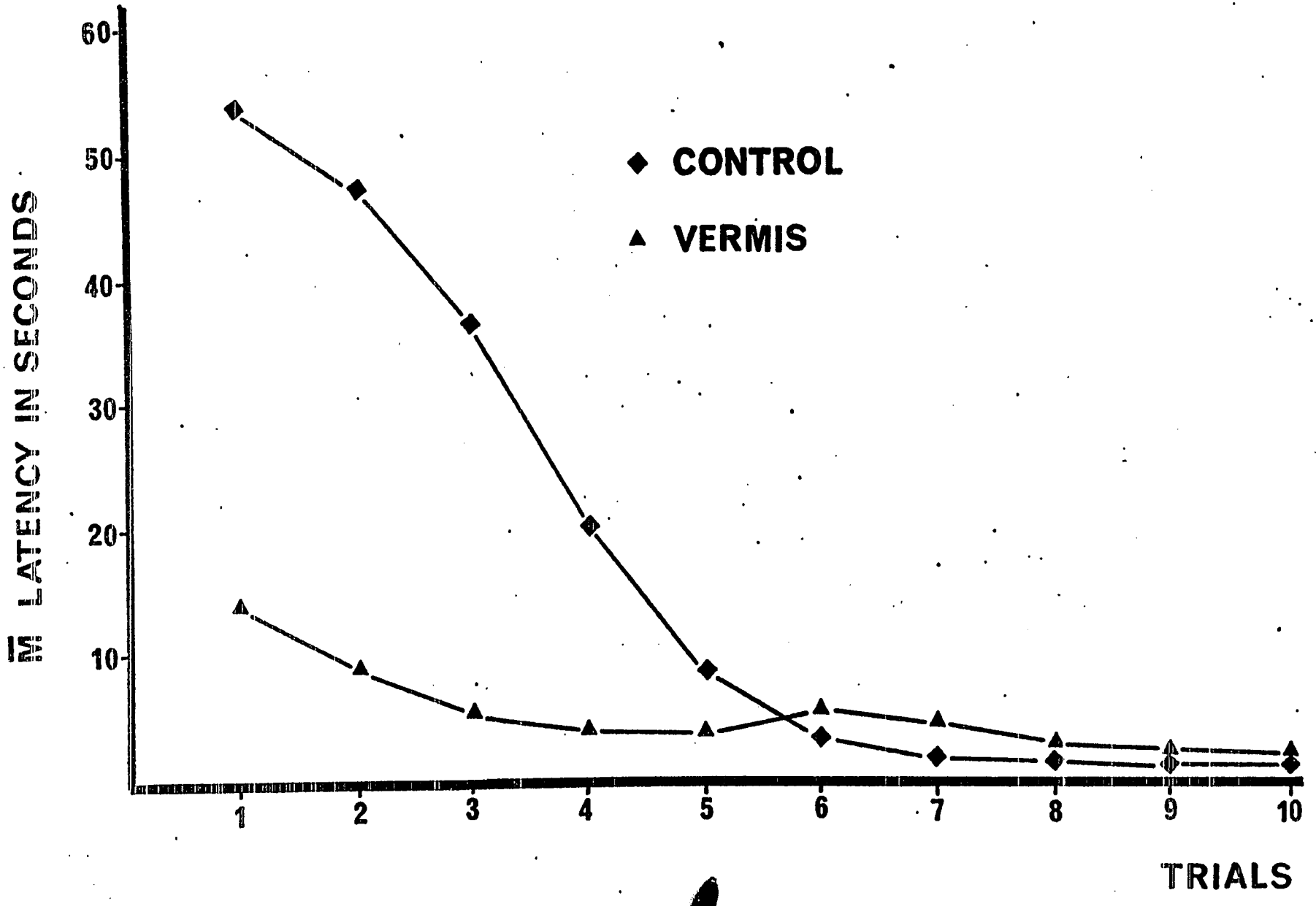

60
50
40
30
20
10
M LATENCY IN SECONDS
CONTROL
VERMIS
1
2
3
4
5
6
7
8
9
10
TRIALS

Figure 5

Passive shock avoidance of rats with vermal lesions and sham-operated rats.

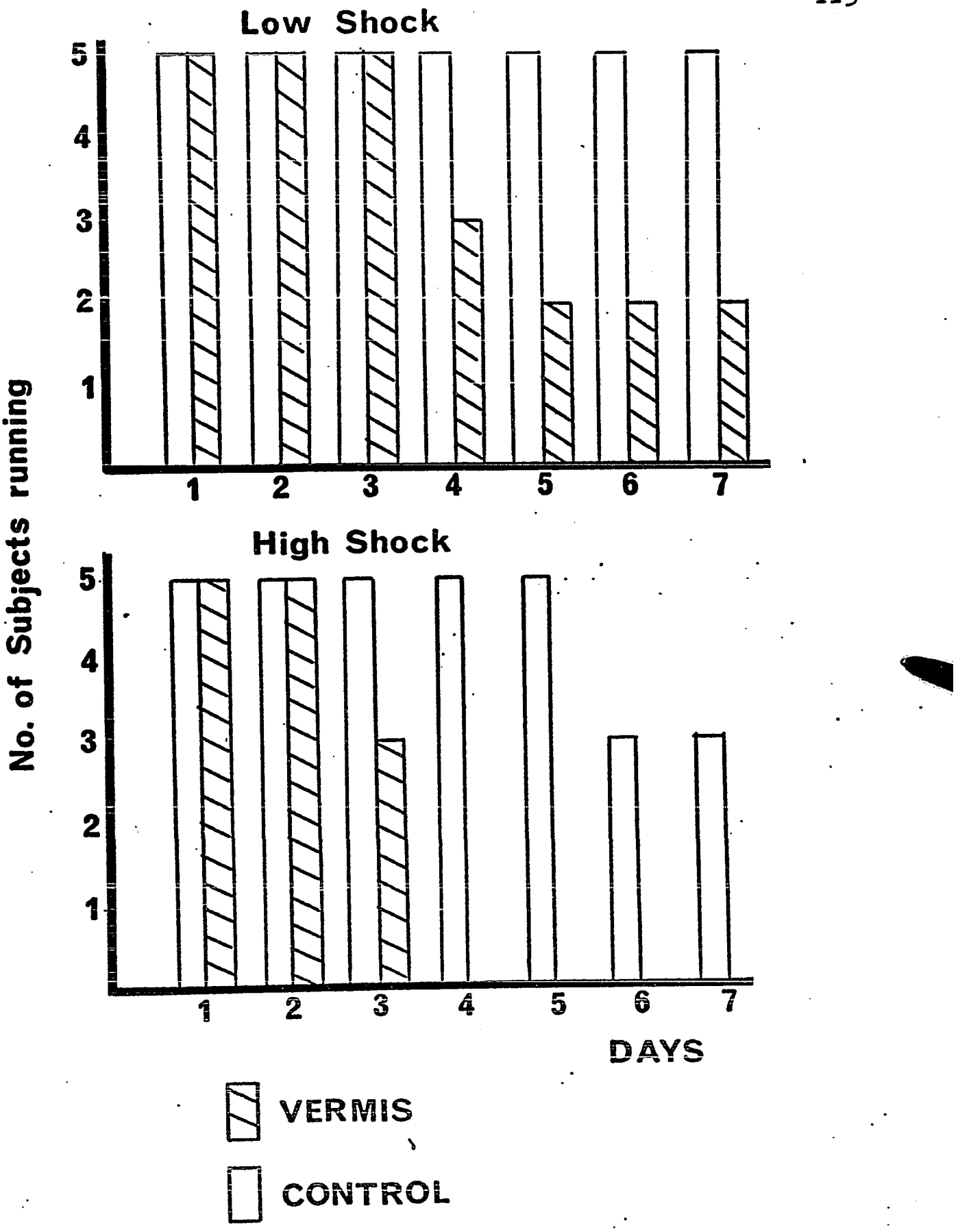
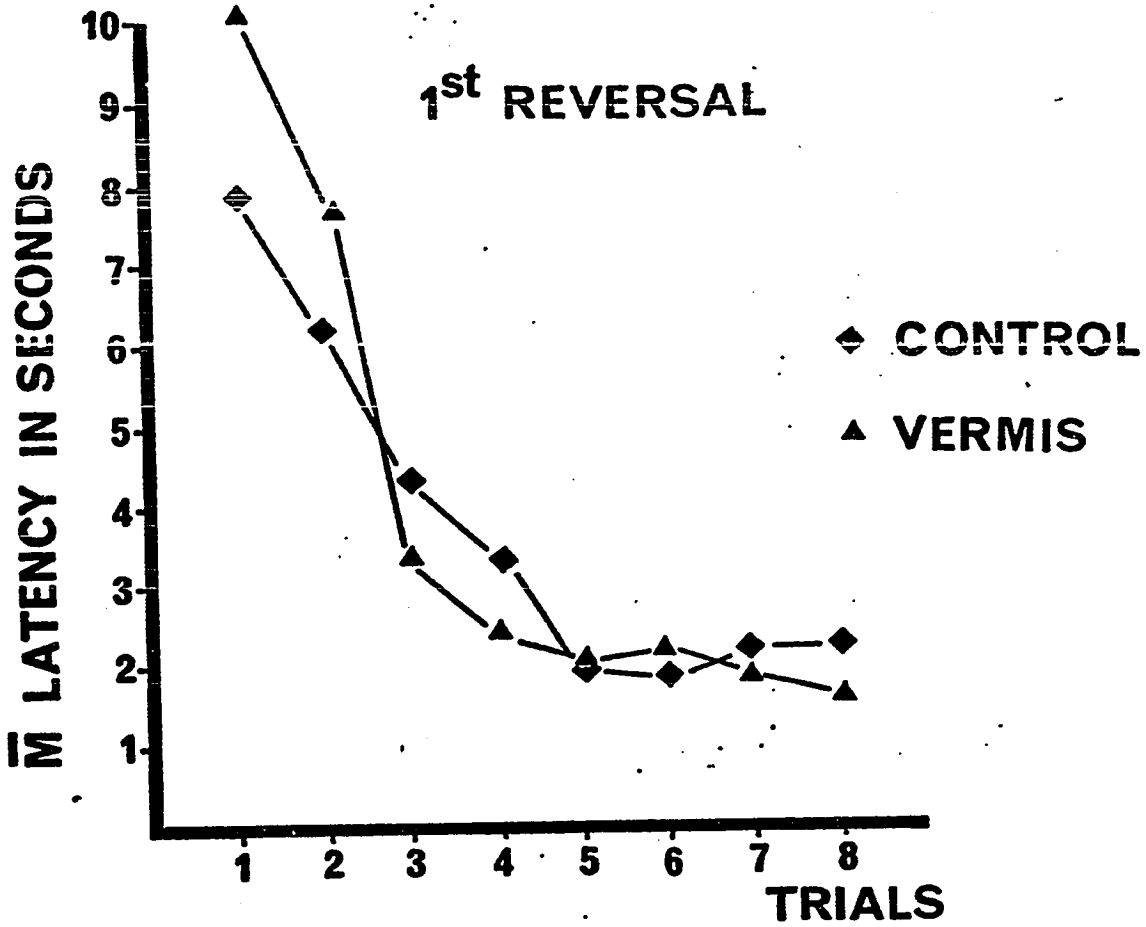

Low Shock
High Shock
No. of Subjects running
5
4
3
2
1
1
2
3
4
5
6
7
DAYS
VERMIS
CONTROL

Figure 6 a and b

Active shock avoidance in the shuttle box by rats with vermal lesions and sham-operated rats on the first (a) and second (b) reversal. The scores are based on the mean of median latencies achieved by the two groups on the daily trials.


1st REVERSAL
CONTROL
VERMIS
M̄ LATENCY IN SECONDS
TRIALS
10
9
8
7
6
5
4
3
2
1
1 2 3 4 5 6 7 8

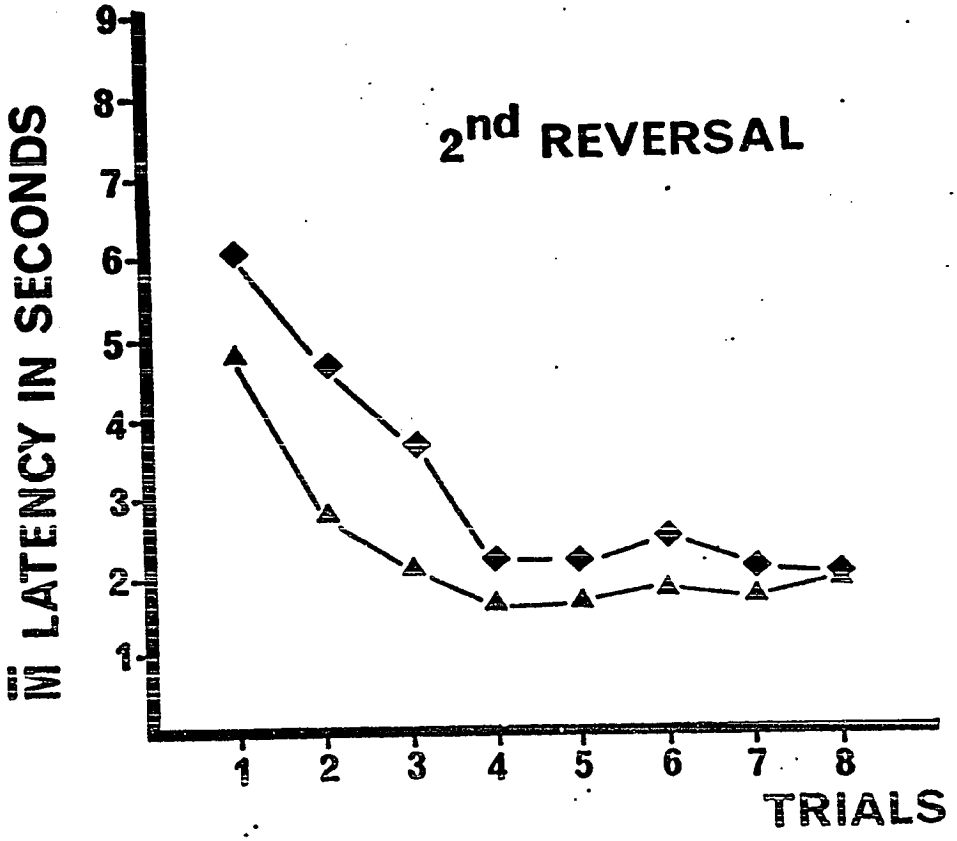

2nd REVERSAL
M̄ LATENCY IN SECONDS
TRIALS
9
8
7
6
5
4
3
2
1
1 2 3 4 5 6 7 8

Figure 7

Representative lesions of the posterior vermis in rats. The density of the grid on the two cerebella to the left and right of the undamaged cerebellum indicates the depth of the lesion; the lesion is deepest in the area of greatest density. The photomicrograph tracings illustrate shallow (a) and deep (b) lesions at their closest approximation to the fastigial nuclei (FN). The dorsal views of the cerebella are based on Zeman, W., and Innes, J. R. M., Craigie's Neuroanatomy of the Rat. New York: Academic Press, 1963.

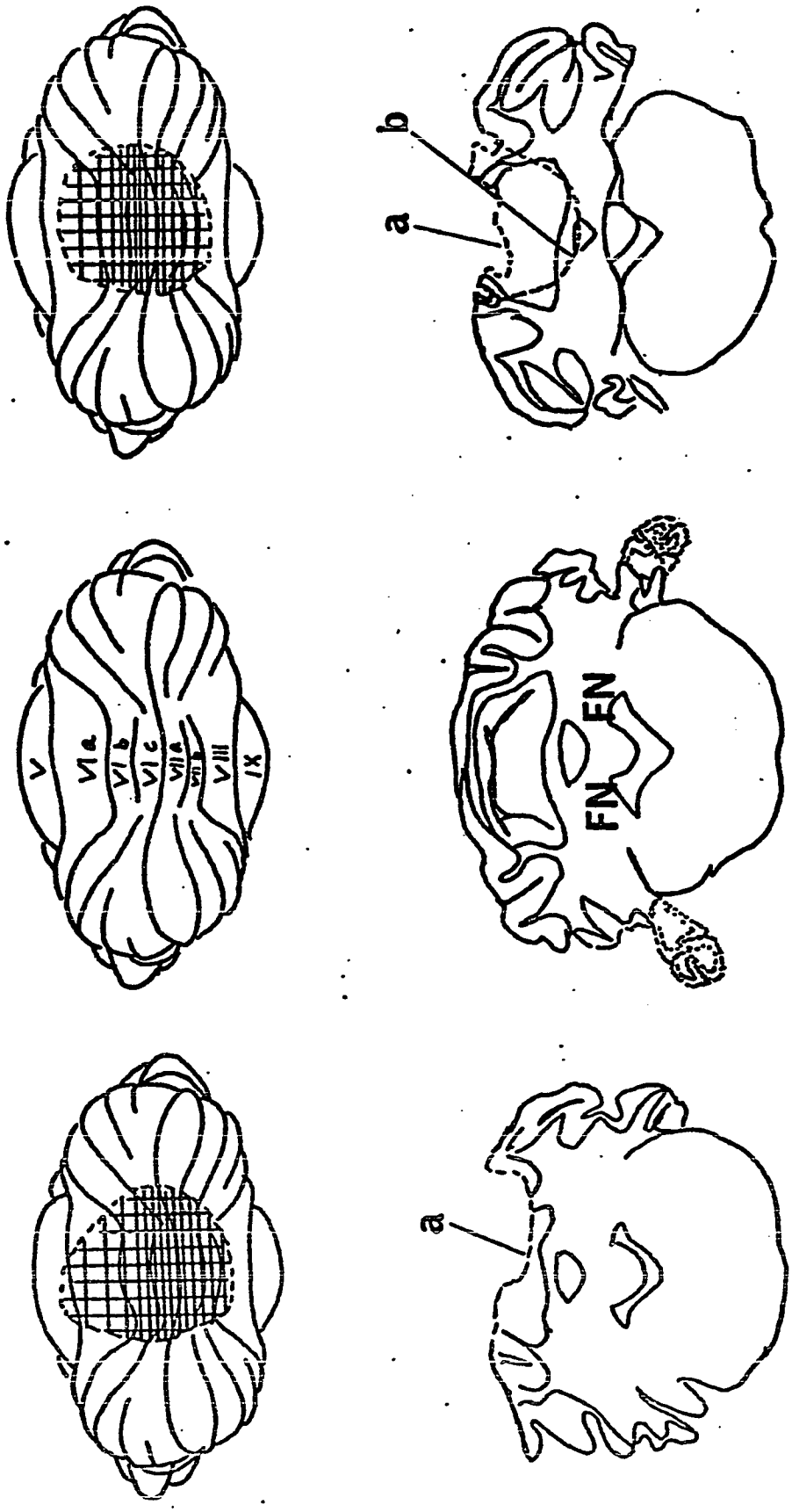
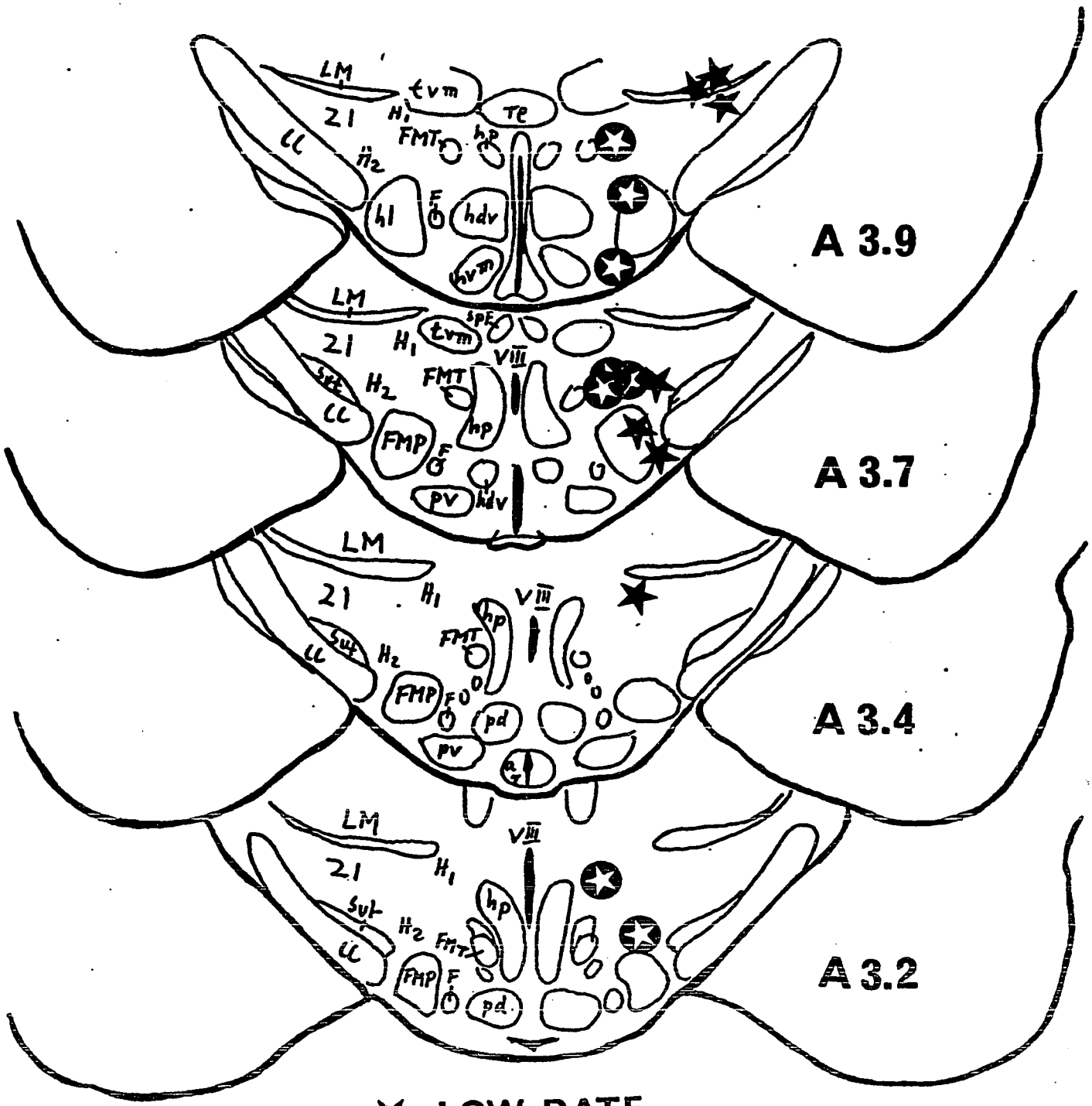

b
a
V
VIa
VIb
VIc
VIIa
VIII
IX
FN
FN
a

Figure 8

Representative electrode sites for low rate and high rate self-stimulators. The sections are based on König, G. F. R., and Klippel, Renate. The Rat Brain. An Atlas with stereotaxic Coordinates. Baltimore: William and Wilkins Co., 1963.


LM
21
H1
FMT
hp
Te
LL
H2
hl
F
hdv
hvm
A 3.9
LM
21
H1
tvm
spE
VIII
FMT
H2
LL
FMP
hp
F
PV
hdv
A 3.7
LM
21
H1
VIII
hp
FMT
LL
H2
FMP
F
pd
PV
A 3.4
LM
21
H1
VIII
hp
FMT
LL
H2
FMP
F
pd
A 3.2
LOW RATE
HIGH RATE